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THE CHCl_3 -PROBLEM



THE CHCl₃ - PROBLEM

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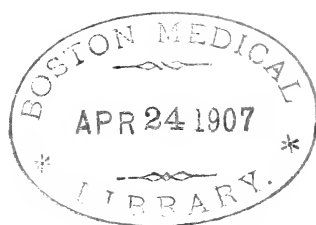
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THE PHYSIOLOGICAL ACTION
OF CHCl₃

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THE CHCl_3 -PROBLEM.



PART III.—*continued.*

RESULTS—*continued.*

§ 62. *THE constant state of normal anæsthesia.*—A constant CHCl_3 -air atmosphere is necessarily associated with a constant physiological effect. If the condition of the part upon which CHCl_3 acts physiologically remains constant, the results of its action in course will continue constant.

But it is characteristic of living tissues that they are sensitive to changes in their nutritional surroundings. CHCl_3 or its products is circulating in the blood. The condition of the blood is consequently rendered abnormal. A tendency to inconstancy is introduced which will manifest itself in favourable circumstances. These are—1, the excessive action of CHCl_3 , which produces a greater degree of disturbance in the

blood than the normal; 2, the initial abnormal condition of the tissues (including the blood) which consequently oppose less than the normal degree of resistance against alteration in their nutritional surroundings; and 3, the length of time over which the abnormal tendency operates.

All living tissues possess certain powers of resistance against changes in the conditions affecting their nutrition. Normal tissues have, *a fortiori*, greater powers than abnormal ones. And some amongst them are more susceptible to particular kinds of nutritional changes than others—*e.g.*, the cerebral and muscular tissues to diminishment of oxygen. The classical example of the constant succession of drops of water upon the hardest rock, shows that a cause in operation, however small its degree of action may be, is necessarily followed by the corresponding degree of its effect, though it may take a very long time before it is manifested to our sense-organs by results. So in the case of living tissues, a slight degree of abnormal nutritional change, if continued long enough, will be followed by a degree of its consequence which is capable of being observed—*e.g.*, the sensitiveness of muscular tissue to stimulation will become diminished, though a considerable interval may elapse before the

impairment of its function, which is synonymous with its abnormal nutrition, is perceived.

Now, this factor—viz., abnormal nutrition—is of the first importance in the investigation of the physiological action of CHCl_3 .

A constant CHCl_3 -air atmosphere is, after an interval, associated with differences in the results accompanying it which do not remain constant, but tend to increase in degree. What is the explanation of the “difference” in results? To avoid the error of mistaking result for effect, it is necessary to analyse the former into its components. These are, 1, the effect of the agent; and, 2, the influence of the part upon which it acts. In the case of nerve-centres, when they are the seat of action, the initial variations which they present are so slight in ordinary healthy individuals that they exert but little, if any, influence on the result. In these circumstances it would, practically, be synonymous with the effect of the agent. But in the case of the blood the initial variations are very considerable, both in respect of its quantity and quality. Its power, therefore, of resisting the adverse influence of agents which directly affect it will present different degrees; and the actual degree of its resisting-power thus becomes one of the

determinants of the actual result, the other being the degree of action of the agent.

The altered condition of the blood, induced by the constant action of the same amount of standard CHCl_3 , or the products of its decomposition, might be assumed to remain constant, on the ground that it does not appreciably interfere with the function of nutrition (apart from the supply of oxygen, which is diminished by the displacement of air in the administration of CHCl_3) during the interval over which the experiment extends. The blood, however, is the source from which all the tissues,—and amongst them, the cerebral centres and the muscles,—derive their nourishment. Now, it is peculiar to living tissues, that if their nutrition is reduced to a given degree below the normal, and maintained at that degree, their vitality or power of resistance tends gradually to diminish. This will be obvious from the following considerations. The abnormal condition of the blood leads to impairment of the nutrition of normal tissues. The condition of these tissues will consequently become abnormal. If, then, abnormal blood continues to supply tissues which are in an abnormal condition through its agency, the degree of abnormality induced in them must

increase. Thus the abnormal condition of the blood remains constant, but the degree of abnormality induced in the tissues tends to increase.

If the degree of CHCl_3 -action is initially anæsthetic, and is continued beyond the period for which it is relatively anæsthetic, it will become associated with the phenomena of narcosis. But the state of anæsthesia will be recovered by reducing, to its relatively proper proportion, the amount of CHCl_3 . Some part, therefore, directly or indirectly affected by CHCl_3 , undergoes a variation of its condition during its action. For the same amount of CHCl_3 has the same degree of effect, and as a variation of result appears, its origin can only be in that part which opposes less resistance to the effect of CHCl_3 . To the data which are concerned in the solution of the CHCl_3 -problem, we have to add (10) the law of diminishing resistance. The part which presents this change of attitude to CHCl_3 is either the blood or the cerebral centres. In the case of the latter, the problem is rendered more intricate by the fact that variation of their condition may conceivably be due, not to the direct but indirect action of CHCl_3 . For there is no proof that CHCl_3 acts di-

rectly on the centres of consciousness. It may be assumed to do so for the purpose of argument. But if it affects those centres indirectly, and its result is maintained at the same degree of intensity, then the secondary phenomena—viz., respiration and pulse-frequencies and muscle-relaxation—should all continue constant. The fact, however, is that they tend to vary. The assumption, therefore, will have to explain how it is that, while the primary result remains constant—*i.e.*, the induced abnormal condition of the cerebral centres—the indirect results undergo variation—*i.e.*, the frequencies of the pulse and respiration tend to increase, and muscle-tone to diminish.

§ 63. *Factors affecting conditions of pulse and respiration.*—The initial frequency, both of the pulse and respiration, is very often rendered abnormal through emotion. In the course of the induction of anæsthesia, those abnormalities tend to disappear. But they do not completely disappear at the onset of automatic respiration and the appearance of the contracted pupil. An appreciable interval, *circ.* 2', elapses before they return to their natural condition. Here we have another example of the indirect results of the cerebral centres continuing after their functions have been suspended. The frequency

of the pulse and respiration should thus be taken 5' after the onset of anæsthesia, when the conditions are (relatively) stable and free from the consequences of possible collateral disturbance. They are then referred to a standard which varies in each individual and is his natural pulse, ascertained in the course of the week before the administration. The knowledge of the course of the pulse during induction, in the case of initial normal hearts, will lead to the avoidance of erroneous inference, if CHCl_3 be administered to those who suffer from weak hearts. Because the strength of the pulse increases and its frequency diminishes during the induction of anæsthesia, the inference might be drawn that CHCl_3 strengthens the cardiac action. But what in reality takes place is this: the action of CHCl_3 , by suspending the functions of the mind, will remove the source of disturbance to the pulse. Consequently, in the course of its methodic administration, the latter will return to its natural conditions. But these may have been masked by the effect of nervousness which is habitual, and on that account overlooked. The CHCl_3 -pulse is, under these circumstances, referred to a false standard—viz., the natural pulse affected by the abnormal condition of nervousness. Thus

the fact that the pulse becomes stronger is not a proof that CHCl_3 strengthens the heart, but it is evidence in favour of the origin of the initial abnormal cardiac action being in the centre of emotion.

The pulse and the frequency of respiration are not constant during the whole period of anæsthesia. But there is a tendency to their constancy in its different stages. Records of the frequency of the pulse and respiration, if they are to possess any value, are therefore to be referred to the "time" at which they are taken. For example, one thousand observations of the pulse and respiration were made at the end of 30' in the course of normal anæsthesia in normal subjects, and the results recorded. The average pulse and average respiration were then assumed to be the normal pulse and normal respiration in CHCl_3 -anæsthesia: but erroneously. The mistake was afterwards rectified by recording the pulse and respiration at the end of every 5' in a second series of observations. It then became evident that the average pulse and respiration differed at different periods, and that the difference consisted in a tendency to their acceleration. This tendency explains partially the discrepancies which exist with regard to the frequency

of the respiration and pulse during CHCl_3 -action. For it is impossible to obtain uniform results unless all the data concerned in their production are alike.

§ 64. *Stability of the state of unconsciousness.*—Automatic respiration is the fundamental sign of suspension of the mental functions. But there are different kinds of unconsciousness—*e.g.*, simple CHCl_3 -unconsciousness and mixed unconsciousness deriving from the $+\text{CO}_2$ -factor co-operating with different degrees of CHCl_3 -action. There are also different degrees of the same kind—*e.g.*, CHCl_3 -anæsthesia and CHCl_3 -narcosis. Now, it may happen that the application of a sensory stimulus immediately after the onset of automatic respiration is followed by partial return to consciousness, as indicated by expiratory moan or voluntary movement, or both. They will be due to the instability of the abnormal condition of the cerebral centres. Sensory stimulation is associated with increase of inspiratory activity. Consequently a relatively large proportion of air is absorbed, resulting in a rapid change in the constitution of the blood. This is obvious in the displacement of duskiess by the natural colour of the complexion in those instances in which the casual factor of the instability is mechanical obstruction.

In normal anæsthesia—automatic respiration, normal colour of the blood and the contracted pupil—the abnormal condition of the cerebral centres is unstable at its onset—*i.e.*, they are sensitive to an increase in the proportion of oxygen in the blood supplying them. This characteristic tends to disappear in the course of anæsthesia, so that at the end of 15' four inspirations of air may be given without any manifestation of returning consciousness. In order to obtain stability of these centres, the state of anæsthesia should be maintained for 2' before the surgical operation is begun. The argument in favour of deep as against light unconsciousness thus falls to the ground. For there will be no necessity for CHCl_3 -narcosis if the state of anæsthesia can be associated at its onset with stability of the abnormal condition of the cerebral centres.

But in the case of what is taken to be deep unconsciousness—automatic respiration, duski-ness, contracted or dilated pupils—sensory stimulation may be followed by manifestations of returning consciousness. Hence the perplexity that will arise from this part of the investigation, unless differentiation be made between the various kinds of unconsciousness that are possible under the circumstances.

These are—1, $+CO_2$ as the chief factor, with an insufficient degree of $CHCl_3$ -action; 2, $+CO_2$ and the anæsthetic degree of $CHCl_3$ -action; and 3, $+CO_2$ and a narcotic degree of $CHCl_3$ -action, the source of the $+CO_2$ being, in each group, some degree of mechanical obstruction. It is in the first group that the difficulty is encountered. The $+CO_2$ -factor being easily removed by oxygen, the cerebral centres, which before sensory stimulation are affected by two agents, producing mixed unconsciousness, will be, after it, influenced by one only, and that a degree of $CHCl_3$ -action which is insufficient to continue the suspension of their functions.

It might be inferred that the return to consciousness will be an indication for the increase of the proportion of $CHCl_3$ in the $CHCl_3$ -air atmosphere. But the inference is not necessarily universal. It can only be drawn if an example presents a relatively efficient state of the respiratory machine. The state of the respiratory machine, however, may be absolutely abnormal, and get associated with partial consciousness. The abnormality is represented by pulmonic congestion, induced either by some fault in the method or by the abnormal displacement of air, necessitated by an inferior

quality of the CHCl_3 in use. In such a contingency it will be obvious that the continuance of the same degree of CHCl_3 -action is contra-indicated (and its discontinuance may be necessitated) by reason of the unfavourable state of the respiratory machine, which, instead of transmitting it to the neighbourhood of the alveoli, tends to its accumulation in the middle and upper air-way.

Some phenomena may be mistaken to be voluntary that are in reality reflex, and the erroneous inference may lead to the continued administration of CHCl_3 where it should be withdrawn, in order to the avoidance of a respiratory overdose. During stable anæsthesia, section of the prepuce is sometimes followed by, 1, prolonged inspiration, accompanied by a crowing noise; and, 2, movements of the lower extremities; and dilatation of the sphincter ani, the more particularly where there is fissure or ulcer, is also occasionally associated with similar phenomena. When they occur the pupil remains pin-point or contracted, thus proving that pain, accompanying an assumed (temporary) return to consciousness, is absent. The fact, however, that the normal state is immediately resumed after the completion of the complication is, in the absence of a certain

contingency, in favour of the continued administration of CHCl_3 during it. The phenomena, however, possess true reflex characters. Thus, the inspiration is unduly prolonged, and the noise accompanying it is explained by the displacement of the base of the tongue, by the increased force of the inspiratory current, resulting in partial closure of the glottis. And the movements of the lower extremities exactly resemble those that follow upon the application of a powerful stimulus to the buttock of a decapitated frog—*i.e.*, the knees are flexed and drawn towards the abdomen, and the heels directed towards the middle line. The contingency consists in the prolonged inspiration being accompanied by the intake of a relative excess of CHCl_3 -vapour into the air-way—*i.e.*, the commencement of the complication coincides with an addition of the maximum atmosphere of CHCl_3 . But the consequences of a respiratory overdose will be avoided by the withdrawal of CHCl_3 during the abnormal inspiration, and by artificially replacing the base of the tongue in its normal position.

§ 65. *The influence of nutritional interference.*—In the constant state of normal anæsthesia, there is no apparent alteration in the constitution of the blood that can be deduced from

variations of its colour, which apparently remains normal. But supposing that foreign substances circulating in the blood exercise an influence on nutrition, the amount of interference induced will, under the circumstances before us, be reduced to a minimum.

That nutritional interference plays an important part in the causation of CHCl_3 -phenomena, follows from the fact that there is no evidence of any (relatively) permanent change in any of the tissues as the consequence of its action upon them. Thus, if we take the cerebral centres, we find that they are extremely sensitive to variations in the proportion of CHCl_3 affecting the blood. A proportion below the anæsthetic will immediately be followed by the phenomena characteristic of the commencement of the return to consciousness. On the other hand, an increase in the normal proportion will immediately be followed by the signs of narcosis, in which state the increased effect upon the cerebral centres is demonstrated by a longer interval separating them from the resumption of their functions as compared with that in the case of anæsthesia. It would seem that, in this respect, CHCl_3 -results differ from those of alkaloids, which appear to affect a change in

the constitution of the nerve-centres upon which they severally act. For their results—*e.g.*, increased frequency of cardiac action in belladonna poisoning and unconsciousness in opium narcosis—continue after the agent which produces them ceases to operate—*i.e.*, has been destroyed. Again, the recovery of the normal functions of a centre, after having been affected by a large dose of an alkaloid, progresses gradually—*e.g.*, it required eighteen hours in the case of a young girl who had inadvertently taken a poisonous dose of belladonna lotion. In CHCl_3 -narcosis—unconsciousness, arrest of respiration—artificial was followed by spontaneous respiration in 75", and the complete recovery of consciousness in 4'.

In the lower degrees of CHCl_3 -narcosis, the blood is more or less dark—*i.e.*, deoxygenated. In so far as oxygen is concerned, it provides a source of nutritional interference with the cerebral centres, the muscles, and the mucous membrane of the stomach. But impaired nutrition leads to impaired function, and before the latter can become normal the various tissues must recover their normal conditions. But there is an intermediate period between the abnormal condition of the tissues, resulting from prolonged insufficient supply of

oxygen to them, and their normal condition, which is associated with efficient oxygenation. During this period functional disturbance will tend to be manifested by headache, lassitude, and sickness. In order to prevent these results, their common cause—viz., the deoxygenation of the blood—is to be reduced to the minimum degree of its action. This will be effected by limiting the degree of CHCl_3 -action to that of anæsthesia, the ideal end-object of the administration of CHCl_3 .

Hæmorrhage occurs in the course of surgical operations during CHCl_3 -anæsthesia. It affects the volume of blood to a larger or smaller extent, and becomes a disturbing factor in nutrition. It is therefore essential to preserve the CHCl_3 -problem from the encroachment which may be made on it by means of this collateral agent.

Hæmorrhage may be either gradual or rapid in its progress, and moderate or severe in its extent. Surface hæmorrhage, which is a negligible quantity in the normal, becomes in the aged and the anæmic an important factor, requiring the accurate adjustment of CHCl_3 to it. The reason is that nutrition in these circumstances is not normal before CHCl_3 is administered. And, consequently, the instability of tissue-life will render it more sensitive to,

or less able to withstand, additional change in their nutritional surroundings, induced by the action of CHCl_3 .

Severe bleeding is immediately followed by secondary reduction of the cardiac function. The proportion of CHCl_3 in such a contingency is regulated by the volume of blood in the main circulation. But in moderate bleeding, extending over a little while, and arrested after the progressive loss has reached an undue degree, the cardiac action will not be immediately reduced. The reduction takes place at a period subsequent to the arrest of hæmorrhage, and is the natural consequence of it. The proportion of CHCl_3 in these circumstances should not be regulated by the actual condition of the pulse, for the reason that it is in a state of transition, and the moment when it will reach its lowest degree of tension is unknown. The ultimate result of the quantity of blood lost is therefore to be anticipated, and the actual proportion of CHCl_3 to be determined, not by what the pulse is, but by what it will be. By following the natural course of events, the variation of the pulse is thus causally dissociated from CHCl_3 -action on the heart. But suppose the proportion of CHCl_3 has not been reduced, a simple result will be rendered com-

plex by a relative respiratory overdose ensuing upon the change of relationship between the CHCl_3 -air atmosphere and the altered state of the respiratory machine. In consequence, both pulse and respiration may fail, and their failure form the starting-point of erroneous inference.

Pallor has thus for one of its ultimate causes external hæmorrhage. When it occurs *where* the tissues are in a condition of initial abnormal nutrition, the rational use of stimulants will be associated with temporary improvement in the condition of the pulse. But because this mode of treatment is successful in one instance, it is not to be inferred either that it is necessary or that it will be followed by the like favourable result in all other instances. For pallor has more than one ultimate cause, and each cause requires particular measures to counteract its effect.

Anæsthesia may be induced without the occurrence of any change of colour of the complexion. The factors necessary for its normal production are, 1, absence of fault in the normal method; and, 2, normal conditions of the subject. Anæsthesia may also be maintained during surgical operation without any change in the colour of the complexion. The necessary factors are—1, absence of fault in normal method; 2, normal

conditions of the subject; and 3, absence of complication arising from the surgical operation—viz., bleeding and sympathetic nerve disturbance. The occurrence of these in different degrees will determine the different degrees of the severity or want of what has been called the shock of the operation. The origin of any simple abnormality is thus referred to the method or the subject of the operation. But the abnormality may be complex. When it is so, it will be essential to analyse it into its components, and to refer each component to its proper cause.

The complex causation of phenomena tends to make the investigation of their origin difficult. And a further source of difficulty that has always to be taken into the consideration of the CHCl_3 -problem, arises from the fact that different subjects present different powers of resisting the same result of the same complication. That is to say, differentiation is to be made between complications occurring in normal and those occurring in abnormal subjects. The analysis of the causes of complication is as follows:—

§ 66. *Fault in method.*—I. There is a less degree than the anæsthetic of CHCl_3 -action present, as determined by diminution of respiratory frequency, accompanied by alteration in

the character of the breathing. If this be not counteracted it will pass into the second stage of returning consciousness, in which the action of the respiratory machine is irregular, and may be attended by voluntary movement or indirect stomach phenomena, the pupil remaining contracted. Dilatation of the pupil characterises the third stage in the return to consciousness, which may also be manifested by verbal expression.

The commencement of the return to consciousness is determined by, 1, less than the normal proportion of CHCl_3 ; or, 2, the proportion being normal, the undue prolongation of the interval between its successive applications.

The former of these factors is made use of towards the completion of the surgical operation. For, instead of maintaining the anæsthetic degree of CHCl_3 -action, a reduction of its amount is made in order to permit of the earliest possible return of the cerebral centres to their normal condition—*i.e.*, in the absence of any contra-indication, there is no rational object in prolonging nutritional disturbance for a longer period than is necessary. II. A respiratory overdose is induced, which leads to pulmonic congestion. It is characterised by reduced range of respiratory

movements and duskiness. It may be due either to a temporary increase of the proportion of CHCl_3 , or, the amount of CHCl_3 being normal, to the abnormal action of the respiratory machine, or to mechanical obstruction in the air-way. III. The physiological action of CHCl_3 is excessive—*i.e.*, some degree of narcosis is present. It is favoured by the dampness of the lint resulting from the relatively short intervals between the successive applications of the CHCl_3 -constituent in hot weather. The shortening of the interval is necessitated by the loss of CHCl_3 through evaporation. And the fault tends to be manifested when the proportion of CHCl_3 is at or near the maximum—*i.e.*, in the later stages of the induction of unconsciousness and the early stages of its maintenance. It is characterised by duskiness and a sluggish and dilated pupil.

The course of these abnormal phenomena is rapid or slow, according to the greater or less degree of action of the "fault." And there is also the possibility that its results may be affected by those of an intervening complicatory cause. Thus, a given degree of an absolute respiratory overdose, which will produce arrest of respiration in 3', may, in combination with mechanical obstruction, cause

it in 1'. Again, owing to the abnormally large size of the tongue, complete mechanical obstruction may occur towards the approach of unconsciousness, and be coincident with the end of expiration. Under these circumstances respiratory arrest will be induced suddenly. Observation, therefore, is constantly needed in order to detect the beginning of abnormality. And the cause (or combination of causes) being isolated, rational measures can at once be put into operation, either to counteract or mitigate its results, before these have reached their highest degree of intensity.

§ 67. *Origin of complication in the patient.*—1, Emotional state; 2, volition; 3, displacement backwards of the base of the tongue; 4, stomachic disturbance; and, 5, primary cardiac syncope.

The results of emotion and voluntary inhibition complicate the early stages of the period of induction. Mechanical obstruction, where the conditions are favourable, intervenes in the later stages. The tendency in all these complications will be to a respiratory overdose, unless the CHCl_3 -constituent of the CHCl_3 -air atmosphere be adjusted to the actual requirements of the intervening abnormal action of the respiratory machine.

Mechanical obstruction is one of the concomitants of CHCl_3 -action. In normal cases its results are slight, and may therefore escape observation. But in abnormal cases — *i.e.*, where there is a predisposing condition, such as weakness of the muscles from emaciation, large tongue, or the abnormal shape of the lower jaw, they are intensified. One of the results of mechanical obstruction is deoxygenation of the blood, an abnormal condition which is prejudicial to the action of CHCl_3 . The degree of danger attending the combination of these two causal factors will vary according to the respective degrees of their action. A comparatively small proportion of CHCl_3 may be highly dangerous in severe degrees of mechanical obstruction, while a comparatively large one, in slight degrees of it, will not be immediately dangerous to life.

Mechanical obstruction may be present alone, or in combination with respiratory overdose or narcosis. It is characterised by duskiness and venous distension. But the condition of the pupil is not affected by it, except during the stage of respiratory interruption, when dilatation rapidly occurs. Its result on the blood — *viz.*, discoloration — disappears very quickly after the removal of obstruction. The extreme

rapidity with which the normal colour of the blood is restored, is the means of differentiating simple mechanical obstruction from respiratory overdose and narcosis, in both which, after the withdrawal of CHCl_3 and the replacement of the base of the tongue, a shorter or longer interval takes place—shorter in respiratory overdose, longer in narcosis—before the blood becomes normally oxygenated. If duskiness continues after the removal of the obstruction produced by the displaced base of the tongue, the possibility of another source of mechanical obstruction has to be taken into consideration. Thus, in surgical operations on the chest, blood may pass through the air-way, or an escape of pus take place into it. There will be, consequently, a less or greater degree of obstruction, according to the less or greater amount of blood (or pus). Duskiness and venous distension will not be materially affected by the replacement of the base of the tongue in its normal position, if it be displaced backwards. In this contingency the head and shoulders of the patient are to be lowered over the edge of the table, so as to exchange the horizontal for the inclined position of the respiratory passage, the base of the tongue being maintained in its normal position. The

change of position allows of the gravitation of the foreign contents of the air-way towards the naso-pharynx. It will be obvious that, gravity being the only means whereby their removal can be effected, there should be no delay in applying it. And it will also be obvious that unless the glottis is patent—*i.e.*, the base of the tongue is in its normal position—the escape of the respiratory contents will be prevented. But the inclined position tends to the backward displacement of the base of the tongue in all states, normal and abnormal. Thus it will be followed by the closure of the glottis. It will be imperative, therefore, to counteract this tendency, and to counteract it efficiently. For the rate of exit of foreign matter is determined by the size of the glottis. And it is essential to get rid of the source of obstruction as quickly as possible. At the same time the size of the glottis determines the amount of air diffused into the alveoli after obstruction is removed, and it is essential that this should be as large as possible, in order to neutralise, as quickly as possible, the results of temporary interruption in the communication between the external air and alveoli, necessitated by the passage of blood or pus through the trachea and larynx.

Mechanical obstruction also occurs as the remote result of complicatory causes. If in these circumstances it is unrecognised, or else only partially relieved, its results will mask those of the initial complication. The complex state thus produced has been taken to be the starting-point of erroneous inferences. For example, pulse-disappearance may be the result of reduced cardiac action, which is one of the results of the original complicatory cause. Mechanical obstruction supervenes and impedes the alveolar circulation, which is also reduced by the reduced action of the heart. The two factors—reduced cardiac action and alveolar obstruction—have no relationship to CHCl_3 -action; but if cardiac failure subsequently occurs, it may possibly but falsely be ascribed to its effect.

It will be essential, therefore, to differentiate between data which are of practical importance and those which are concerned in the construction of hypothesis. For if pulse-failure occur, and the following inferences be drawn—1, that it is the consequence of cardiac weakness; and, 2, that cardiac weakness is the direct result of CHCl_3 -action,—the notion, if entertained, that “muscle-relaxation” is primarily concerned in its recovery, is not likely to be treated with

that regard which is its due, because treatment is limited to stimulation of a depressed heart. But supposing that the heart is weakened by the assumed depressant action of CHCl_3 , it will follow, from the fact that recovery takes place in some instances of its occurrence, that cardiac weakness, thus induced, varies in degree in different instances. Can the actual degree of it be determined at the onset of pulse-failure? If this be impossible, the rational treatment will be to make the surroundings of the heart as favourable as possible to the gradual recovery of its normal function. And this will be effected by counteracting the result of "muscle-relaxation" on the air-way—viz., by replacing and maintaining the base of the tongue in its normal position, with the prime object of supplying air to the alveoli, and, consequently, of removing the impediment—viz., alveolar obstruction—in the way of the recovery of the cardiac function.

§ 68. *Stomachic disturbance.*—There are two kinds of stomachic disturbance—the indirect and the direct. The indirect kind may appear in the early stages of the period of induction, where it has its origin in the imagination. It may also appear in the later stages, and is then due either to some fault in method or to the poor quality of CHCl_3 in use. Instead of the

uninterrupted transition from consciousness to anæsthesia, in which the functions of the external senses are first suspended, retrogression occurs, and the recovery of external consciousness may be associated with stomachic manifestations.

Anæsthesia once attained, it is necessary, in order to its maintenance, to continue the normal CHCl_3 -air atmosphere, but the proportion of CHCl_3 in it must be progressively diminished in accordance with the law of diminishing resistance. If the continuity of the normal mixed atmosphere is interrupted, either by increase or diminution of the normal proportion of CHCl_3 , a deviation from the normal course of anæsthesia will ensue. In the latter case, its tendency is to the return of consciousness. The first indication of this abnormality is decreased frequency of respiration, the action of the respiratory machine remaining regular. The second phase is characterised by the appearance of irregularity in its action, accompanied by manifestations of volition. During this stage, indirect stomachic phenomena may appear. But when they do so, they are not accompanied by pallor (with the exception of those instances in which direct stomachic disturbance coincides with returning consciousness). The treatment

consists in restoring the normal proportion of CHCl_3 , which, however, has to be effected gradually. But inasmuch as all states presenting stomachic phenomena are not alike, and as the presence of CHCl_3 , even in the lowest proportion, may be contra-indicated in direct stomachic disturbance, its indiscriminate use will be followed by different consequences. Because, in some instances, the continuance of CHCl_3 is followed by the reappearance of automatic respiration, and in others by its arrest, is no argument in favour of its peculiar action—*i.e.*, in the sense in which peculiarity is used. But perplexity will necessarily arise when different states, having only some phenomena in common, are taken to be exactly alike (*i.e.*, all presenting the same phenomena), and treated in the same way. To remove perplexity, its source is to be exposed and the tendency of it counteracted. If, therefore, a rational conclusion is drawn with the assistance of all the data which enter into it, the possibility of error will be avoided, and the different results which follow upon the same treatment of apparently similar states, will be shown to be derived from different causes or combinations of causes.

Direct stomachic disturbance is due to interruption to the progress of the digestive function.

Where preparation is possible, and efficiently carried out, its cause—viz., undigested food in the stomach—is absent. But it happens that immediate surgical operation is necessary in cases where preparation is impossible. And thus the study of the phenomena associated with stomachic disturbance becomes essential.

There are three stages in the course of a typical example of direct stomachic disturbance. The first is marked by irregular movements of the intestines. The second is characterised by reduced action of the respiratory machine—stomachic inhibition of the respiratory centre—and pallor, the result of stimulation of the vaso-motor centre. This stage varies in the length of its duration, and it is accompanied by the contracted pupil. It is followed by the act of vomiting, which constitutes the third or final stage of direct stomachic disturbance.

Though it may be anticipated, yet the moment of its occurrence cannot be determined. Hence the rule of maintaining the state of the respiratory machine free from embarrassments that are contingent upon the undue negative or physical action of CHCl_3 , so that it shall always be ready for its reception.

The mechanism of the act of vomiting is complex. It begins with intense stimulation of the

peripheral ends of the vagus in the stomach. The powerful stimulus is transmitted along the vagus nerve to the vomiting centre in the floor of the fourth ventricle, whence it is distributed to the respiratory and vaso-motor centres. Stimulation of these centres is followed respectively by functional arrest of respiration and fall of blood-pressure. But the incidence of respiratory arrest is characteristic. It takes place at the end of a full inspiration. Its occurrence at this phase in the action of the respiratory machine leads to the temporary fixture of the diaphragm. That contracted muscle, supported by the expanded lungs, forms a fixed plane, between which and the contracting abnormal muscles the stomach is compressed. The expulsion of the stomachic contents will be immediately followed by the return of the respiration and complexion to the normal, which is rapidly effected.

But this abnormal action of the stomach is sometimes characterised by variety. The successive stages may be rapidly encompassed, and within a very short interval after its beginning the complication may end in sudden arrest of respiratory movements. Thus the occasional occurrence of this phenomenon gave rise to the hypothesis of the physiological action

of CHCl_3 on the respiratory centre, while in the comparatively larger group of instances presenting a well-defined second stage, pallor is arbitrarily taken to be the proof of the direct and dangerous influence of CHCl_3 on the heart.

Now, the act of vomiting may be interrupted. The antecedent requisite condition is arrest of the action of the respiratory machine at the end of a full inspiration. The factors that prevent full inspiration are—1, sufficient degree of mechanical obstruction; 2, respiratory overdose; and, 3, pulmonic congestion. If either of these (or a combination of any two, or all of them) is present when the act of vomiting is about to take place, two causes will be in opposition—viz., a tendency to a full inspiration, and the abnormal condition of the airway or of the lungs, which becomes a causal factor in the altered circumstances of the action of the respiratory machine, tending to prevent it. And arrest of respiratory movements at some stage in the course of the act of inspiration will consequently ensue. If the abnormal condition, which thus becomes a causal factor, is removed at once, the progress of the act of vomiting will be resumed. If, on the other hand, it is not removed, or there

is undue delay in its removal, abstract consideration of the circumstances leads to the conclusion that the abnormal states, both of the respiratory machine and circulation, will not remain the same as they were at the moment of respiratory arrest, but will become intensified in degree—*i.e.*, pulmonic congestion will be increased, as also the distension of the right ventricle, which will be manifested by general venous distension.

In the course of CHCl_3 -unconsciousness, the conditions of the several components of the respiratory machine are not necessarily normal. But if they are normal they will not be absolutely constant, by reason of the variations in the CHCl_3 -constituent. Thus in anæsthesia, mechanical obstruction or a temporary respiratory overdose may coincide with functional arrest of respiratory movements. In narcosis, pulmonic congestion, either alone or in combination with mechanical obstruction, or a respiratory overdose, may be present and impeding full inspiration.

Hence, in view of the possibility of the occurrence and rapid progress of the stomachic complication, it is essential that the conditions which may become causal factors opposing it shall be absent. Thus pulmonic congestion

will be prevented by limiting the physiological action of CHCl_3 to the degree of anæsthesia. Mechanical obstruction will be removed by replacing and maintaining the base of the tongue in its normal position. But it will be impossible to avoid a temporary respiratory overdose under the circumstances at the beginning, without adequate warning, of the act of vomiting. For the addition of CHCl_3 is necessary in order to maintain the CHCl_3 -air atmosphere at its relatively normal strength. But the CHCl_3 -constituent passes from its highest to its lowest degree of concentration as the consequence of its evaporation and absorption. Thus the former will be most potent if, 1, the amount is comparatively large—*i.e.*, during the early stages of anæsthesia; and, 2, if it is comparatively small, when functional arrest of respiration coincides with or occurs soon after its application.

Thus functional arrest of respiratory movements may take place during a favourable or an unfavourable condition of the air-way. In the former there is no impediment to the act of vomiting, consequently that natural function will proceed without interruption. But in the latter the presence of respiratory obstruction introduces a flaw in the mechanism of the

complex act of vomiting. Arrest of respiratory movements will not immediately be followed by the expulsion of the stomachic contents: and it is this circumstance that will point to the site of the disturbing factor. When functional respiratory arrest is not immediately followed by expulsion of the contents of the stomach, the base of the tongue is to be replaced and maintained in its normal position, and the contents of the air-way artificially expelled. The air-way being thus restored to its normal condition, a full inspiration will be followed by, 1, functional respiratory arrest; and, 2, expulsion of the stomachic contents.

But if a respiratory overdose is not efficiently removed as soon as possible, it will be followed by physiological pulmonic congestion, which will increase in degree proportionately to the increase of delay in the conveyance of air to the alveoli. Thus, what is at first a temporary obstruction, will subsequently become converted into a relatively permanent one. In this respect the state induced by delay resembles that which results from the concurrence of functional arrest of respiration with the pulmonic congestion of CHCl_3 -narcosis. But they differ in another—viz., that the blood is of normal colour before the occurrence of res-

piratory arrest in the one, while in the other it is discoloured. Now it is this difference that explains the difference in the length of interval that elapses before recovery is effected by means of artificial respiration. Where the blood is normal before the onset of respiratory arrest, the interval is found to be comparatively short; but where the blood is discoloured before the onset of respiratory arrest, it is found to be comparatively long. It is obvious that the limit within which the reduction of physiological pulmonic congestion is to be effected will be determined by the resisting power of the right ventricle. The object of artificial respiration is to relieve its over-distended condition. Under the circumstances this can only be done gradually. For the compression of the chest is not synonymous with the expulsion of all the contents of the air-way, but only a part of them. The recoil of the chest will be followed by an intake of air, which is arrested at a greater than the normal distance from the alveoli. It can only reach its destination by diffusion. But in order to this an interval is necessary. And it is this interval that accounts for the gradual conveyance of air to the alveoli, for the gradual aeration of the blood in the distended terminals of the pul-

monic artery, for the gradual diminution in the tension of its main trunk, and consequently for the gradual removal of increased pressure in the right ventricle.

From the fact that direct stomachic disturbance has two degrees of relation to the respiratory centre—viz., inhibition of its action and functional arrest—two modes of onset of respiratory arrest during CHCl_3 -unconsciousness are possible: 1, sudden, either at the end or during a fall of inspiration; and, 2, more or less rapid—the consequence of the reduced action of the respiratory machine being complicated either by a respiratory overdose or mechanical obstruction, or both.

But whether sudden or rapid, respiratory arrest is necessarily followed by changes in the circulatory system. These will be prejudicially affected by antecedent abnormal conditions of some of the components of both the respiratory and circulatory systems. Thus a fall of blood-pressure below the requisite degree is not associated with disappearance of the pulse, if at the moment of its onset the respiratory machine is normal both as to its state and function, and the circulation is normal. Suppose, however, that the same degree of fall of blood-pressure occurs under the abnormal

conditions of physiological pulmonic congestion and increased arterial tension, the pulse will disappear. It will be essential, therefore, in any given instance of it, to isolate, 1, the origin of fall of blood-pressure; and, 2, the abnormal conditions determining its result on the pulse. The origin of fall of blood-pressure, where it is associated with an abnormal condition of the respiratory centre, is in stimulation of the vaso-motor centre. These two centres—the respiratory and vaso-motor—are intimately connected by extensive nerve-channels. Between and below them, in the floor of the fourth ventricle, is the vomiting centre, which directly communicates with both of them. Functional arrest of the action of the respiratory centre is effected by a stimulus arising in the stomachic terminations of the vagus, and conveyed by it to the vomiting centre, whence it is distributed to the respiratory and vaso-motor centres. But the degree of fall of blood-pressure, which appears simultaneously with respiratory arrest, is not, in normal conditions of the pulmonic artery and the main vascular system, sufficient to cause the disappearance of the radial pulse. For the alveolar circulation, undisturbed by vaso-motor complication, continues to supply the left ventricle,

and thus returns the main mass of the blood, which has been diverted into the portal system, into the general circulation. The rate of the alveolar circulation, therefore, will determine the volume of the radial pulse; and a factor which disturbs the former will exert a corresponding result upon the latter. Such a factor is distension of the pulmonic artery, which is associated with a diminished rate of alveolar circulation without vaso-motor complication; with vaso-motor complication this reduced rate of alveolar circulation leads to a relative insufficient supply to the left ventricle, and consequently to the disappearance of the radial pulse.

In case of the inhibited action of the respiratory centre, blood-pressure falls simultaneously with and is proportioned to it. As long as there is no impediment in the way of efficient aeration, so long will the radial pulse maintain its natural though abnormal degree of volume. But the function of aeration may be disturbed by mechanical obstruction—an incidental consequence dependent upon an indirect result of vaso-motor complication—or by a respiratory overdose. If, then, either of these causes is supposed to operate during stomachic inhibition of the respiratory centre,

the radial pulse will manifest the following changes. First, there is increase of its tension, which is of longer or shorter duration, according to the less or greater degree of the action of the disturbing factor; and secondly, there is a rapid disappearance of its beat.

The relation of the failure of the pulse to the causation of "states of crisis" that are characterised by abnormal condition—either inhibited action or functional arrest—of the respiratory centre is thus of secondary importance. The radial pulse may fail after respiratory movements cease, or the failure of both radial pulse and respiration may appear to occur simultaneously. But it does not necessarily follow that the pulse is not present in the innominate, because it cannot be felt in the radial artery. The object of practical importance is the removal of obstruction in the way of the alveolar circulation, and this is effected by restoring free communication between the outside air and the alveoli.

In this group of instances of respiratory arrest, the respiratory centre is known to be the seat of abnormal action. The analysis of CHCl_3 -action leads to the separation of its negative and physical from its physiological effect. There is evidence of its purely physical action in the

respiratory overdose, and pulmonic congestion is one of the components of CHCl_3 -narcosis. Both respiratory overdose and pulmonic congestion may be present before, or may appear subsequently to, reflex arrest or inhibition of the action of the respiratory centre. On the other hand, these reflex actions may occur during the normal state of the respiratory machine. The inference, therefore, is not that CHCl_3 exercises a peculiar physiological effect on the respiratory centre, thus minimising or neglecting altogether the influence of the different states under which arrest of respiratory movements occurs, but that these different states exert, in so far as one or other of their components is concerned, a determining influence in the causation of a temporary suspension of the action of the respiratory machine. The erroneous inference that CHCl_3 has a peculiar effect on the respiratory centre is supported by the experience derived from the results associated with the same degree of its action in different instances, or in different stages of the same instance. For example, a given degree of CHCl_3 -action is not associated with abnormality of the respiratory machine in the early stages of anæsthesia. In the course, however, of anæsthesia, the action of the respiratory machine becomes inhibited, and the same

degree of CHCl_3 -action will inevitably, sooner or later, be associated with its arrest. The deduction that CHCl_3 causes respiratory arrest through its paralysing influence on the respiratory centre, is drawn without regard to the influence of the more important factor in its complex causation—viz., inhibited respiration. In other words, no analysis is made of the conditions of the parts which are affected in the production of the phenomenon whose causation is under investigation, and the conclusion is drawn from insufficient data.

But there are other groups besides the ones already indicated, of instances of respiratory arrest which possess each its own characteristic causal factor. Thus the study of its causation is rendered still more intricate. Voluntary arrest or inhibition of the action of the respiratory centre, during the period of the induction of unconsciousness, may be complicated by mechanical obstruction or a respiratory overdose; during the stage of unconsciousness CHCl_3 -narcosis may be complicated by mechanical obstruction; and rapid arrest of the action of the respiratory machine, from exhaustion of its motor-power, is one of the terminals of the narcotic degree of CHCl_3 -action.

§ 69. *Primary cardiac syncope*.—The occurrence

of this phenomenon is rare. It is associated with some inherent abnormality of the heart—*e.g.*, 1, imperfect development of the left ventricle co-existing with hypertrophy of the right, in an infant 8 months old; 2, dilatation of the right ventricle, in a youth of 19 years, indirectly caused by a solid tumour situated between the larynx and œsophagus, and compressing both; 3, degeneration of the cardiac muscle in a man, aged 36, who had been the subject of long-continued suppuration from the right kidney. Each of these instances was characterised by the same sequence of phenomena—*viz.*, sudden disappearance of the pulse, accompanied by full dilatation of the pupil, empty veins and muscle-collapse, and followed by gradual decline of respiratory movements. The immediate replacement of the base of the tongue is not followed by any alteration in the size of the pupil. But it is essential in order to demonstrate the attitude of the respiratory centre. For the continued action of the respiratory machine is, in the abnormal condition of cardiac failure, dependent upon freedom from obstruction.

There is no intimate connection between the action of the heart and the function of the respiratory centre. But there is between the

respiratory and vaso-motor centres, so that stimulation of the latter will immediately be followed by a corresponding change in the former. The most intense degree of its severe stimulation is known to be followed by a rapid decline of the function of the respiratory centre, which is manifested by the rapid decline of respiratory movements. The attitude of the respiratory centre, therefore, will determine the origin of the fall of blood-pressure. And, inasmuch as variations in the activity of the respiratory centre are reflected in corresponding variations of respiratory movements, the reason for preserving these movements from being impeded will be obvious when it is considered that, 1, the respiratory muscles are suddenly deprived of their blood-supply; and, 2, they are in the least favourable condition for supplying the extra work which is necessitated by the presence of an obstacle in the performance of their duties—*e.g.*, increased expiratory effort to expel the contents of the air-way through a narrow glottis.

§ 70. *Complications arising in connection with surgical operations.*—The immediate results of surgical operations may be, 1, hæmorrhage; and, 2, reflex stimulation of the vaso-motor centre. In the case of hæmorrhage from the naso-

pharynx reaching undue proportions, the head and shoulders are to be lowered, and the mouth left open with a gag, in order to favour the passage of the blood to the outside, while measures are being taken to arrest its flow. But these are sometimes anticipated by the natural arrest of the hæmorrhage through secondary syncope, when the blood is to be quickly removed from the pharynx, as a precautionary measure before the replacement of the base of the tongue in its normal position. For there will be a chance, on the one hand, of blood entering the larynx; on the other, there is obstruction to the passage of air from the outside to the alveoli, and it may be temporarily complete. Judgment will have to be exercised, as well as care in manipulation, with regard to the supply of air to the alveoli on these occasions.

One of the consequences of long-continued surface hæmorrhage during CHCl_3 -action, appears in a tendency to cardiac debility. (The nutrition of the cardiac muscle is affected through the alteration of the blood produced by CHCl_3 , and in course of time the defect will assume appreciable dimensions.) The tendency will be favoured by the initially weak power of the heart which is associated with the state of emaciation. Such a concurrence

of factors will determine the judicious use of cardiac stimulants: their end-object is to enable the heart to tide over a temporary difficulty. Consequently the application of them is to be limited to that degree of result which suffices for the amelioration of those emergent conditions which necessitate their use.

For this reason—stimulation consumes the energy of the heart. But the initial energy of the heart in these instances is less than the normal, and it has already been considerably encroached upon. There is, therefore, the danger of too rapidly consuming what remains of the cardiac energy. And the consumption of energy, when it is not restored, will be followed by rapid depression.

§ 71. *Vaso-motor depression*.—Reflex stimulation of the vaso-motor centre is consequential upon the application of a stimulus to some part of the sympathetic nervous system. It is, therefore, to be anticipated during surgical operations on the abdominal organs and in the deep-seated region of the neck. Thus, in intussusception, the CHCl_3 -air atmosphere should be replaced by air 20" before the manipulation of the affected intestines, with the object of, 1, insuring the freedom of the alveolar circulation from what would be a relative obstruction, if CHCl_3 were continued in

normal amounts; and, 2, of favouring the return of the blood from the portal to the main circulation. The degree of stimulation of the vaso-motor centre varies with the degree of the intensity of the stimulus. The minor degrees are associated with acceleration of respiratory frequency (already increased as the result of CHCl_3 -action); and the major degrees with rapid decline of respiratory movements, which become limited to the abdomen, and in the severest instances undergo a temporary suspension. It is essential to include the minor degrees of reflex vaso-motor stimulation in the study of agencies affecting the cardiac function in the course of CHCl_3 -action, in order to explain the temporary disappearance of the pulse in the major. And it is requisite that there shall be no interruption to the progress of the phenomena composing the state of vaso-motor complication—*i.e.*, the action of the respiratory machine is to be free from obstruction and the circulation of the blood in the alveoli unimpeded. For, supposing that the return of the blood is checked by approaching stasis of the alveolar circulation, the disappearance of the pulse, instead of being temporary, will become relatively permanent—(*i.e.*, until the alveolar circulation is restored to the normal).

And it will be obvious that undue delay in the return of the radial pulse in these circumstances will form a false support for the hypothesis that CHCl_3 directly weakens the action of the heart.

As the result of reflex stimulation of the vaso-motor centre, there is immediate fall of blood-pressure. And as the result of fall of blood-pressure, there is a corresponding reduction of cardiac power, in accordance with the fundamental law of the equation of the degree of cardiac action to the volume of blood in the main circulation. In the most intense degrees of stimulation of the vaso-motor centre, the power of the heart is temporarily reduced to a minimum. The reduced power of the heart is thus secondary to fall of blood-pressure, and an indirect result of stimulation of the vaso-motor centre. It is conservative in its object, and it automatically returns to the normal on the return of the blood to the main circulation. But its rate of progress is necessarily slow, because the alveolar circulation, upon which it is dependent, is affected by a temporary interruption in the normal supply of air to the alveoli, consequent upon rapid decline of respiratory movements. It is clear, therefore, that in this contingency there will be no need for artificial cardiac stimulation.

The fall of blood-pressure in the main circulation is followed by increased tension in the portal system. And after the components of these systems have severally adjusted themselves to temporary abnormal conditions, there will come into operation a natural tendency to the normal redistribution of the blood. Thus, the blood will pass through the portal vein and inferior vena cava into the right heart, which propels it to the pulmonic capillaries. But its further passage through the lungs can only be effected by aeration. If this should be obstructed, the current of the blood will be diverted through the superior vena cava into the veins of the upper part of the body. Consequently the superficial veins will become distended in that region.

Associated with reflex stimulation of the vasomotor centre are—1, dilatation of the pupil; and, 2, muscle-collapse. Both appear simultaneously with, and present variations of degree proportionate to, the degree of fall of blood-pressure. Thus, in intense degrees of the latter the pupil is fully dilated, and the degree of muscle-relaxation extreme, while in less severe instances the pupil is more or less dilated, and the degree of muscle-relaxation greater or less. But in all instances the dilated pupil retains its sensitive-

ness to the action of light. Inasmuch as both these phenomena occur in fall of blood-pressure, consequent on primary syncope or cardiac exhaustion, the inference is very probable that they are not directly related to reflex stimulation of the vaso-motor centre.

Muscle-relaxation, however, becomes of practical importance, in respect that it favours the backward displacement of the base of the tongue, and, therefore, mechanical obstruction in the air-way, which thus becomes a remote result of the original complication. But mechanical obstruction tends to arrest the alveolar circulation, on which the recovery of the pulse is dependent; by cutting off the supply of air to the alveoli. And the heart, after endeavouring to overcome a progressively increasing obstacle, during which it diverts some of the blood passing through its right side into the tributaries of the superior vena cava, finally ceases to beat, and presents post-mortem, an over-distended right ventricle, and either a left one empty or else containing a small amount of black blood. It is not often that the same agent is related to two results which are antagonistic to each other. But vaso-motor complication will provide an example of this rare relationship. It causes a temporary

displacement of the blood. And to the return passage of the blood from the portal system to the main circulation, it opposes an obstacle by indirectly producing alveolar stasis.

The indications of recovery from the results of reflex stimulation of the vaso-motor centre, occurring during CHCl_3 -anæsthesia—the rational means of treatment being supposed to be in operation—viz., the head and upper part of the body lowered so as to allow of gravity assisting the current of blood in the vena portæ, and the base of the tongue maintained in its normal position—are, 1, the rapid return of the dilated pupil to the condition of normal contraction; and, 2, a faint alteration of the colour of the complexion. No artificial emptying of the contents of the air-way is needed. For this takes place naturally through diffusion in the interval during which the two vital functions are adjusting themselves to their new surroundings. The return of the blood to the main circulation is necessarily slow. But it is essential on that account to possess the knowledge that it is not in the least degree being impeded.

Free communication between the external air and alveoli being achieved and maintained, the gradual progress towards the normal is characterised, first, by the increase of the range

of abdominal movements; and secondly, by the extension of respiratory movements to the lower thorax. These gradually increase and progressively affect the middle and upper parts of the thorax. But though the action of the respiratory machine is considerably advanced, yet the pulse will not be as yet perceptible at the wrist. The index of the returning power of the heart is for this stage the progressive increase of coloration of the complexion.

The recovery of the respiratory centre from secondary disturbance is associated not with a normal condition of the respiratory muscles, excepting the diaphragm, but with the abnormal condition of the immediate and complete interruption to their blood-supply. Before the intercostals can assume their ordinary functions, it is necessary that they shall be supplied with blood, and this is gradually effected through the intermediation of the diaphragm. The alveolar circulation is dependent, together with air in the alveoli, upon the continued action of the diaphragm. And upon the alveolar circulation the return of the pulse is dependent, first on the larger arteries, and afterwards on the smaller ones. Thus, in this, as in all other complications, there is no *statu quo*; and if rational means are not promptly and efficiently

put into operation, the reduced action of the heart will be subsequently opposed by alveolar obstruction, which tends to cause its permanent failure. The hypothesis that the heart is directly weakened, in pointing to its stimulation, favours delay in restoring the normal conditions of the alveolar circulation. The consequence of this delay will, therefore, support its physiological value.

The occurrence of vaso-motor depression is not associated with undue alarm during consciousness. But when it happens during CHCl_3 -anæsthesia, it is apt to be regarded with a high degree of danger which does not properly belong to it. There are, however, these differences in the conditions of the muscles and the conscious centres presented by the state of consciousness and anæsthesia. In the former, normal muscles are suddenly bereft of their blood-supply, and consequently reduced to a condition of profound relaxation; the functions of the centres of consciousness also are immediately, but only temporarily, suspended. If, then, the base of the tongue is displaced backwards so as to completely obstruct the air-way, there will be sufficient air below the seat of obstruction to carry on the alveolar circulation until the centres of con-

sciousness begin to resume their functions, when respiratory obstruction is spontaneously removed. But in the case of anæsthesia no such assistance is afforded to the action of the respiratory machine. The muscles, which are already in an abnormal condition of relaxation, present, when suddenly deprived of their blood-supply, a degree of relaxation amounting to collapse. They do not, consequently, recover their tone as rapidly as if they had been in an initial normal condition. And the consequence is that mechanical obstruction, which in the state of anæsthesia and in the supine position is an invariable result of muscle-collapse, remains unrelieved, and will continue so until it is artificially removed.

The results of intense pain are those of vaso-motor depression accompanied by full dilatation of the pupil. The argument might therefore be adduced that the vaso-motor phenomena, instead of originating in the terminals or one of the main branches of the sympathetic nerve-system, arise indirectly from the great sensory centres of the brain. This presupposes, however, the state of returning consciousness—*i.e.*, a condition of the sensory centres equal to the reception of stimuli—and further, considerable progress in the return, because the condition

of the cerebral sensory centres is one of the determinants of the result on them of stimulation, and it becomes more favourable in this respect the nearer complete consciousness is approached. There are three stages in the return to consciousness. The first indication is diminished frequency of respiration. This is followed by its irregularity. Dilatation of the pupil occurs in the last stage. But vaso-motor phenomena appear when the action of the respiratory machine is automatic and the pupil is normally contracted. Now, automatic respiration precludes consciousness, and the contracted pupil is the measure of the lowest or anæsthetic degree of CHCl_3 -action. The question, however, might be put, Is this degree sufficient to withstand the most powerful sensory stimuli? The answer is supplied by experience, which teaches that the occurrence of vaso-motor phenomena is not universal, but only occasional, in anæsthesia, that the most severe surgical operations are not necessarily followed by manifestations of returning consciousness, and that vaso-motor phenomena, when they appear, are invariably associated with sympathetic nerve-stimulation. Thus, sensory stimulation as a sufficing cause is excluded. But there is a further possibility. "Would

these occasional instances happen if the degree of CHCl_3 -action were higher than the anæsthetic—*i.e.*, during CHCl_3 -narcosis?" And this leads to the investigation of vaso-motor complication affected by abnormal conditions.

The return of the blood from the portal to the main circulation is impeded when the alveolar circulation is obstructed. The immediate cause of obstruction is defective aeration of the blood. One of the causes of the latter is the excessive proportion of CHCl_3 in the CHCl_3 -air atmosphere which is administered. And one of its results is physiological pulmonic congestion. In the state of narcosis, which varies in degree according to the degree of excess or overdose of CHCl_3 , the degree of alveolar obstruction varies directly with the degree of pulmonic congestion on the one hand, and with the degree of discoloration of the blood on the other. If, then, a fall of blood-pressure takes place—and it is matter of experience that falls of blood-pressure do occasionally take place during duskiess—*i.e.*, deficient oxygenation of the blood, with which pulmonic congestion is necessarily associated,—two factors will be present affecting the return of the blood to the general circulation. First, there is the natural flow of the blood towards

the right side of the heart, whence it is propelled into the pulmonic artery; secondly, there is an impediment, less or greater, in the alveolar circulation. These causal factors, when simultaneously in action, oppose each other. And it is this opposition that prevents the heart, which has previously been subjected to some degree of exhaustion, resulting from pulmonic congestion, and the power of its action is now reduced in proportion to the degree of fall of blood-pressure, from gradually recovering its normal function.

A high degree of CHCl_3 -action signifies a corresponding degree of alveolar obstruction. Supposing that vaso-motor reflex action is affected by the state of CHCl_3 -narcosis, so that the results of the same degree of the peripheral stimulus are diminished in greater or less degree, according to the greater or less degree of narcosis. The greater the degree of narcosis, the greater will be the over-distension of the right side of the heart, and the greater the diminution in the results of reflex stimulation of the vaso-motor centre—*i.e.*, the less the fall of blood-pressure. The heart, while in an induced abnormal condition, will be affected by the consequence of some degree of a sudden fall of blood-pressure. And

the result of this upon its impaired function has to be taken into consideration. Is the heart likely to recover as readily from a temporary state of disturbance in this abnormal, as it does in its normal, condition? Has the abnormal condition any influence upon its recovery, and, if so, what is that influence? But assuming that the heart is not seriously affected—*i.e.*, the degree of over-distension is moderate, and its duration, antecedent to the onset of fall of blood-pressure, is short—the following difficulty presents itself—*viz.*, there is an impediment to the return of the blood to the main circulation. But the intensity of the impediment increases in proportion to the degree of narcosis. The argument against the use of the higher degrees of CHCl_3 -action is therefore conclusive; for the greater the impediment to the alveolar circulation, the greater will be the interval required for its removal, which possibly may have to be effected by the application of artificial respiration; and upon the length of this interval the maintenance of the function of the heart depends.

The other causes which affect aeration of the blood are—1, some degree of mechanical obstruction; and, 2, temporary respiratory overdose. Either or both of these factors may

concur with sudden fall of blood-pressure. In the case of the former, it is removed by replacing the base of the tongue in its normal position, and the progress of the complication will subsequently continue without interruption to its normal termination. But in the case of the latter, the replacement of the base of the tongue will not always be followed by the gradual return of respiratory movements. For the course of the complication is interrupted by it, and the interruption will be manifested by commencing distension of the superficial veins. If the degree of respiratory overdose be slight, the natural process of diffusion will effect its dissipation before an undue degree of venous distension is attained (always supposing that the air-way is maintained normally patent). But if it be intense, as manifested by the rapidity with which venous distension increases in intensity, its artificial expulsion will become necessary. In such instances, a single but efficient compression of the lower thorax will be followed by the return of abdominal movements, and the disappearance of venous distension.

Thus, vaso-motor complication may be masked by pulmonic congestion—one of the components of the state of narcosis—and by respiratory

overdose or mechanical obstruction during anæsthesia. When it occurs during any one or a combination of any two or all of these abnormal conditions, the resulting state will be either a practically simultaneous disappearance of the radial pulse and respiratory movement, or the pulse disappears first and is followed by very rapid arrest of respiratory movements. The phenomena of pulse-failure and respiratory arrest in such contingencies are not single or isolated, but members of two sets or states of complication which oppose each other. It would be, therefore, logically erroneous to regard them as individual or even as the fundamental phenomena of the physiological action of CHCl_3 , without disproving that the abnormal condition of alveolar obstruction, which is the common result of pulmonic congestion, mechanical obstruction, and respiratory overdose, has no subsequent influence on the recovery of the cardiac function, as well as that those several causes have no influence in the production of respiratory arrest.

Reflex stimulation of the vaso-motor centre is not in normal conditions associated with danger, and its principal result—viz., diversion of the blood into the portal system, is auto-

matically removed. In CHCl_3 -anæsthesia the complication pursues its normal course, except in those instances in which it is temporarily interrupted by respiratory overdose or mechanical obstruction, which are easily put out of operation. But when it occurs during CHCl_3 -narcosis, the abnormal condition of the alveolar circulation, which in itself is not immediately dangerous if uncomplicated, will become so relatively to the change in the distribution of the blood. Thus, neither the limited degree of narcosis nor vaso-motor complication is able to cause permanent arrest of the heart's action. But their opposed action tends to do so, and will actually effect it, unless relief is given to the embarrassed condition of the heart within an interval, the length of which is determined by, 1, the initial power of its resistance; and, 2, the degree of exhaustion to which it has been subjected.

There are two sets of phenomena associated with primary fall of blood-pressure. The one is derived from reflex stimulation of the vaso-motor centre, the other from cardiac syncope. In anæsthesia there is no difficulty in distinguishing between these states, because the differentiating factor—viz., the abnormal action of the respiratory machine—is the simple result

of the complicatory cause. In narcosis, however, there is a difficulty, arising from the additional disturbance which is induced in the action of the respiratory machine by a cause which is independent of the complicatory one. In these instances the differentiation can only be made with the assistance of artificial respiration: 1, if recovery is effected, and the pulse regains its natural strength, it will follow that the heart has not been directly affected by CHCl_3 ; 2, if, on the contrary, recovery does not take place, the natural condition of the heart may be normal or abnormal. The evidence of the cardiac origin of the fall of blood-pressure will be forthcoming in some local abnormality of the heart.

§ 72. *Isolation of the phenomena of the physiological action of CHCl_3 .*—The error underlying the treatment of the CHCl_3 -problem consists in the arbitrary separation of prominent phenomena from their intimate surroundings. Conclusions are drawn from an individual phenomenon—always a precarious logical procedure—and not from a set of phenomena or a “state.” The selected phenomenon may chance to be the fundamental one. But there is no assurance that it is so. Thus in the case of pallor: it is a direct manifestation of reflex stimulation of the

vaso-motor centre; it is also a direct result of primary cardiac syncope; again, it is a secondary result of stomachic inhibition of the respiratory centre. It will be obviously impossible to conclude from pallor alone, without the assistance of the phenomena accompanying it. And the irregularity which has been ascribed to the action of CHCl_3 is thus traced to one of its sources in the action of different causes acting simultaneously with it. But as in other spheres, so in that of CHCl_3 , as much help can be derived from the study of minor as of major degrees of intensity of the same phenomenon. Such help, however, will be precluded by the use of the higher degrees of CHCl_3 -action. For these not only mask the complication at its first appearance, but they also tend to interrupt its natural progress. As the consequence of such interruption, respiratory arrest or pulse-failure may occur. Now, the circumstances under which these phenomena appear are not uniform. Their mode of onset varies. The phenomena accompanying them vary. The antecedent conditions of the components of the respiratory and circulatory systems and of the pupil vary. And the phenomena subsequent to their appearance vary. But notwithstanding all these variations, the

arrest of action of the respiratory machine is ascribed to paralysis of the respiratory centre, and pulse-failure to the peculiar action of CHCl_3 on the heart. All instances of these phenomena are arbitrarily assumed to be of the same nature. They are not, as they should be, classified into groups according to the greater or less resemblance of the characters which they possess in common. There is no explanation of the difference in the size of the pupil accompanying respiratory arrest. And some causal factors are actually present, and yet their significance is either ignored or else they are excluded as being unequal to produce the phenomenon under investigation. But in the case of arrest of respiratory movements, the question has, first of all, to be decided, What are the phenomena that are associated with paralysis of the respiratory centre?—*i.e.*, what is the conduct of the circulatory system, and what is the attitude of the pupil in that (assumed) abnormal condition?

Confusion will necessarily arise if no discrimination is made between different causes producing the same result. CHCl_3 may cause, but only under certain circumstances, either arrest of the action of the respiratory machine or pulse-failure. But it has not been proved to

act directly either upon the respiratory centre or upon the heart. On the other hand, respiratory arrest and pulse-failure may be caused by agents independently of CHCl_3 -action while operating simultaneously with it. And the nature of their causation is known to be direct. It will be essential, therefore, that the set of phenomena, and the variations which each of its components undergo, in the successive stages of CHCl_3 -narcosis, be known, in order to avoid the error of ascribing to it results which proceed from other causes.

But confusion will be increased by treating those instances of respiratory arrest or pulse-failure as of simple origin which are actually due to a combination of causal factors, one of which is a CHCl_3 -product. In such complex instances it becomes necessary, in order to avoid the error of ascribing the whole when only a part of the result is due to the action of CHCl_3 , to analyse the complex phenomenon into its simple components, and to isolate the one which is of CHCl_3 -origin. Thus the part acted by it in combined causation will be defined. Lastly, the CHCl_3 -result is referred either to its negative, physical, or physiological action.

The first stage in the solution of the CHCl_3 -

problem is thus completed. It is concerned with the removal of phenomena which do not belong to it. The means by which this is effected are, 1, the normal induction of anæsthesia; and, 2, the maintenance of the constant state of normal anæsthesia. For it is clear that abnormalities deriving from causes operating simultaneously with, but independently of, CHCl_3 , can only be isolated if the results of the latter are defined. The second stage consists in the examination of the phenomena which are associated respectively with the lowest degree of CHCl_3 -action or anæsthesia, and its higher degrees or the different degrees of narcosis. The results of the examination lead to the performance of certain experiments. And upon conclusions derived from these the theory of the physiological action of CHCl_3 is founded.

PART IV.

THE THEORY OF THE PHYSIOLOGICAL ACTION OF CHCl_3 .

§ 73. *PURE CHCl_3 -results.*—The CHCl_3 -problem is complicated by two difficulties, one of which is extrinsic and the other intrinsic.

The extrinsic difficulty consists in the inclusion of phenomena which either do not belong to CHCl_3 , or else are only its partial results. Thus arrest of respiratory movements may be caused by several different agents acting collaterally with, but independently of, CHCl_3 . It may also be caused by the combined action of CHCl_3 with a complicatory cause. And it may be the result of CHCl_3 -action which causes it in two different ways. It will be essential, therefore, to exclude simple non- CHCl_3 -results; and in the case of complex results, of which CHCl_3 is one of the causal factors, to isolate the part which it plays in their production.

The intrinsic difficulty consists in not distinguishing between the physical and physiological action of CHCl_3 . Arrest of respiratory movements is caused, under favourable circumstances, by its physical action alone. It is obvious, therefore, that before arrest of respiratory movements can be ascribed to the physiological action of CHCl_3 , the result of its physical action is to be excluded; and that in case those two different actions combine to cause a complex respiratory arrest, their degrees are severally to be isolated, and the influence which each exercises on the result defined. The exclusion of, 1, causes acting independently of CHCl_3 , and, 2, its physical action, removes obstacles in the investigation of the relation between the physiological action of CHCl_3 and the causation of some instances of respiratory arrest.

Similarly, all the other pure results of the physiological action of CHCl_3 in its different degrees are isolated. The scope of the inquiry is then extended to the determination of the relation which these results have, in the first place, to each other, and in the second, to the action of CHCl_3 . Differentiation is made between direct and indirect results. The isolation of the former leads to the detection of

the effect of CHCl_3 -action. In respect of the latter a result, more or less intimately related to CHCl_3 -action, is shown to be an intermediate cause whose direct result has dangerous tendencies. If, now, an indirect is mistaken for a direct result of CHCl_3 -action, it follows that all inferences derived therefrom are necessarily fallacious.

§ 74. *The different degrees of CHCl_3 -action.*—The degree of its physiological action varies according to the amount of CHCl_3 which is absorbed into the blood. The quantity of the cause determines the amount of the effect which it produces. But the effect itself is not separately manifested: for a cause acts upon some form of matter which is in either an active or passive condition. The influence of the part which is affected by CHCl_3 enters, therefore, into the result, which is the manifestation of its action. It is important not to mistake the “result” for the “effect” of a cause. The part acted upon may be for all practical purposes constant. On the other hand, it may be a variant. So that in some instances less of the cause is able to produce the same degree of result than in others.

The importance of this analysis of the result into, 1, the effect of the cause, and, 2, the

influence of the part acted upon, is not so obvious in the case of variations of the action of the respiratory centre or of the normal heart. But it is fundamental in the case of the blood, which presents initial differences both in quantity and quality. Thus, an agent acting on the respiratory centre so as to increase its activity, may be said to be responsible for the whole of the resulting accelerated action of the respiratory machine—*i.e.*, the condition of the centre does not modify the result. Here result and effect may be regarded as practically synonymous. And they will remain so, provided the condition of the respiratory centre does not undergo any change. In the case of the blood, however, there is no such initial stability of condition as is presented by the centre of respiration. The influence of the blood, in opposing less or greater resistance to the effect of a cause acting upon it, thus becomes an important factor in the determination of the result. And its value is to be accurately estimated.

The anæsthetic degree of CHCl_3 -action (which is not constant for all subjects, but varies according to the quantity and quality of the blood) is always associated with the same set of phenomena. These form a state of the subject to

which the term anæsthesia is restricted. Higher degrees than the anæsthetic are called narcotic, and the corresponding states of narcosis are differentiated as to their degree by the degree of dilatation of the pupil. Comparisons instituted between the states of anæsthesia and narcosis on the one hand, and on the other between different degrees of the latter, lead to the acquisition of data which are auxiliary to the isolation of the effect of CHCl_3 .

In order to reach the blood, which is the seat of its action, CHCl_3 mixed with air is conveyed by the act of inspiration to the terminal bronchioles, whence it is diffused into the alveolar region. The displacement of a proportion of air in the mixed atmosphere breathed tends to impair the function of aeration. In anæsthesia, this tendency is counteracted by the increased activity of the respiratory machine, following upon stimulation of the respiratory centre. The stimulus is either a diminution of the normal volume of oxygen, or an increase of CO_2 in the blood. Sufficient oxygen is thus automatically supplied to attain the object of normal respiration—viz., the normal aeration of the blood. It is possible that there may be in anæsthesia a slight discoloration of the blood. But if there is, it is indistinguish-

able by the naked eye. It is also possible that oxygen within a given limit may be abstracted from the blood without producing a change of its colour.

But in narcosis, the result of the amount of air displaced by CHCl_3 upon the function of aeration is not counteracted by the increased activity of the respiratory machine. The function of aeration is consequently impaired, and the degree of its impairment is measured by the degree of the discoloration of the blood.

Thus the negative action of CHCl_3 comes to play a very important part in the production of the state of narcosis. Its results, consequently, will have to be taken into consideration and separated from the purely physiological results of the narcotic degree of CHCl_3 -action. For it is impossible to produce the latter without at the same time bringing the former into operation. The results of the negative action of CHCl_3 are—1, distension of the pulmonic artery; 2, stimulation of the respiratory centre; and, 3, nutritional interference, consisting of a diminution of the normal supply of oxygen to the tissues generally.

§ 75. *The induction of anæsthesia.*—The proportion of CHCl_3 in the CHCl_3 -air atmosphere is gradually but progressively raised from

the minimum to the maximum. The physical action of CHCl_3 is counteracted by the use of small amounts, repeated at frequent intervals. And the introduction of error into the result from this source is thus avoided.

In a typical example the frequency of respiration is immediately accelerated. The degree of acceleration increases in a direct proportion to the increase of the CHCl_3 -constituent of the CHCl_3 -air atmosphere. And as the frequency tends to increase, the character of the respiratory movements tends to become regular. In the course of the accelerated and regular action of the respiratory machine, the pupil tends to contract. The rate of contraction is gradual and progressive up to the lowest degree—viz., the pin-point pupil. Coincident with the appearance of the pin-point pupil, the character of the action of the respiratory machine presents a sudden change. Its range becomes increased, the individual movements are equal, and the rhythm is regular. Automatic respiration, the fundamental sign of unconsciousness, is attained.

There is no alteration in the colour of the complexion. And the pulse is slightly increased in frequency.

But all examples are not typical. Variations

of the action of the respiratory machine may occur early or late in the course of inducing anæsthesia. Thus its range may become reduced by voluntary inhibition of the function of the respiratory centre. The temporary variation does not preclude but determines a corresponding modification in the management of the CHCl_3 -air atmosphere. If, therefore, the action of the respiratory centre continues in a condition of inhibition during the administration of CHCl_3 , the conclusion is that, whatever the influence of the latter may be, whether direct or indirect, its effect on the centre is less powerful than that of volition.

Again, the action of the respiratory machine may become obstructed. This complication arises from a fault in the method of administration. Though small quantities of CHCl_3 are used at frequent intervals, in order to prevent the occurrence of a respiratory overdose, it nevertheless results from error in estimating the length of the interval. And as temperature determines the rate of evaporation of CHCl_3 , the error is more prone to be committed in hot than cold weather. The indications of commencing respiratory overdose are, 1, diminution in the range and frequency of respiratory movements, and, 2, duskiness. They tend to undergo reduction

when the proportion of CHCl_3 in the CHCl_3 -air atmosphere is diminished. And they disappear when the proportion of CHCl_3 reaches its normal amount, the range and frequency of the action of the respiratory machine being then normal.

This complication presents diminished frequency of respiration, associated with more than the normal proportion of CHCl_3 . Respiratory frequency is determined by change induced in the respiratory centre. But in the former complication diminished frequency of respiration accompanies less than the normal proportion of CHCl_3 . It is impossible, therefore, that CHCl_3 should cause both these variations in respiratory frequency through its direct influence on the respiratory centre. But it is possible that it does not cause either of them through the same channel.

§ 76. *Phenomena of normal anæsthesia*.—The onset of automatic respiration is accompanied by the following phenomena: 1, increased frequency of respiration, 28; 2, efficient action of the respiratory machine, indicated by the normal colour of the blood; 3, the contracted or pin-point pupil; 4, muscle-relaxation; 5, slight increase in frequency of the pulse, M. 73, F. 75.

At the commencement of the state of normal anæsthesia there is no appreciable alteration in muscle-tone, and sensori-motor reflex-action is normal. The first phenomenon to appear is acceleration of respiratory frequency.

A cause in operation is at once followed by its effect upon the part which is the seat of its action. In the case of CHCl_3 there is this difficulty. It can only be administered with air, and therefore a certain portion of air is necessarily displaced in the process. But the displacement of air results in the absorption of less than the normal quantity of oxygen. And a diminution of the normal volume of oxygen in the blood is invariably associated with, and is a possible cause of, stimulation of the respiratory centre. Thus the negative action of CHCl_3 will supply a reason for the acceleration of respiratory frequency. But this does not preclude the possibility of CHCl_3 also acting as a respiratory stimulant, on the supposition that it is taken into the blood and carried to the respiratory centre. The results, however, of experimentally increasing or diminishing the amount of CHCl_3 are nullified by the following circumstance: the variation affecting the CHCl_3 -constituent is associated with a corresponding variation of the quantity of air. Thus, if the

proportion of CHCl_3 be increased, there will be an additional increase to the accelerated frequency of respiration; but at the same time there will be a further reduction of oxygen in the blood. And if the proportion of CHCl_3 be diminished, there will be a proportionate reduction of respiratory frequency; but at the same time there will be a corresponding increase of the volume of oxygen in the blood. The question whether CHCl_3 has a direct or indirect action on the respiratory centre is thus unanswerable by reason of its negative action. The only direct way by which it can be determined is to estimate the amount of air which is displaced by the vapour of CHCl_3 , and ascertain the degree of increased frequency which it produces. Thus, if the amount of displaced air is represented as A , and the degree of increased frequency corresponding to it as y , then, if the amount of CHCl_3 necessary to produce A is associated with a greater degree of respiratory frequency than y , and represented as x , $x-y$ would remain as the part of accelerated respiration properly belonging to the physiological action of CHCl_3 . But as the amount of air displaced by the vapour of CHCl_3 is at present an impossible datum, the investigation of the relation between the physiological action of CHCl_3 and

the respiratory centre will perforce have to be conducted by indirect channels.

§ 77. *Variations occurring in the course of normal anæsthesia.*—The only phenomena remaining constant during anæsthesia are the efficient action of the respiratory machine and its consequent—viz., the normal colour of the blood. The phenomena presenting variations are—1, the accelerated respiration, which tends to increase; 2, the pulse, which also tends to increase in frequency; 3, muscle-tone, which tends to become diminished; and 4, sensori-motor reflex-action.

It is necessary to consider the relation of these several variations to the action of CHCl_3 . After the induction of anæsthesia there is, in normal examples, a period of comparative stability, lasting for 30', after which the tendency to variation in the phenomena above enumerated will be manifested. The degree of the tendency, however, which is slight at the commencement of its operancy, does not remain constant, but gradually increases as the duration of anæsthesia is prolonged. Thus the respiration and pulse become more accelerated, and muscle-tone and sensori-motor reflex-action become more abnormal the longer the anæsthetic degree of CHCl_3 -action is continued;

and, further, the degree of variation in the former is directly proportionate to the duration of the latter.

The variation in the frequency of the pulse invariably appears after variation in the frequency of the respiration. They stand, therefore, in the relation of antecedent and consequent.

A diminution of normal muscle-tone obviously affects the results obtained by stimulating either the motor-nerve or the sensory-nerve in sensorimotor reflex-action. Under this circumstance the condition of the nerve-centre and the altered conductivity—if there be any change—of the motor and sensory nerves remain at present unknown. But it is to be recollected that they do not present any change from the normal in the first stage of the course of anæsthesia.

These two variations—viz., of respiratory frequency and of muscle-tone—may be regarded as being most intimately connected with the prolonged anæsthetic degree of CHCl_3 -action. And from the relation subsisting between them, it may be inferred that they are either the results of the same cause, which is CHCl_3 itself or a CHCl_3 -result, or one of them is the cause of the other.

Now it is found necessary, in order to maintain the state of normal anæsthesia—*i.e.*,

automatic and efficient respiration and the contracted pupil—to progressively diminish the proportion of CHCl_3 in the CHCl_3 -air atmosphere which is administered. For the amount of CHCl_3 which is “anæsthetic” for a particular stage, becomes “narcotic” for those stages that succeed it, the degree of narcotic action being greater the further it is removed from the stage of anæsthesia. The same degree of CHCl_3 -action is thus perceived to be eventually associated with different results. One of these results is a tendency to respiratory acceleration. On the other hand, if the same amount of CHCl_3 is progressively diminished, a similar tendency is manifested. But there is a characteristic difference in the rate at which increase of respiratory frequency progresses in these different examples. The rate of increase is greater in those instances in which the amount is maintained constant than in those in which it is progressively diminished.

Now the same amount of cause is followed by the same amount of effect, whatever may be the condition of the part which it affects. But in the case of CHCl_3 , the same degree of action, when continued beyond a given period, is associated not with the same but with different results. And the differences are manifested

both by the degrees of the phenomena which are already in existence—viz., respiratory acceleration and diminution of muscle-tone—and by the appearance of new kinds—viz., the discoloration of the blood and venous distension.

When the set of phenomena or “state” varies, the amount of the cause remaining the same, the inference is that some part acted upon by it undergoes a variation of its condition. For the components of the result are—1, effect of the cause ; and, 2, influence of the part affected. This part, which may be the seat of the direct or indirect physiological action of CHCl_3 , thus takes a prominent place in the solution of the problem. And its isolation becomes the object of investigation. The variation which it undergoes in offering a gradual but progressive diminution of resistance to the anæsthetic degree of CHCl_3 -action, forms the foundation of the “law of diminishing resistance.” And this law may be subsidiary to the discovery of the physiological action of CHCl_3 .

§ 78. *Frequency of complications during the induction and maintenance of the state of anæsthesia.*—In one series of 1000 consecutive cases, complications occurred 125 times. They do not present the same characters. Nor does

the same complication always present the same degree of severity. The phenomena composing any one state of complication do not invariably accompany CHCl_3 -action, and therefore they cannot logically be ascribed to it.

There are three possible sources of the disturbing factor: faulty administration, the presence of a variant condition, and the intervention of an independent cause acting simultaneously with CHCl_3 .

The method of administration may possess an inherent fault—*e.g.*, the Rapid Method, which induces an undue degree of both the negative and physical action of CHCl_3 . Or a fault may appear in the Graduated Method, which is designed to limit the physiological action of CHCl_3 to the degree of anæsthesia—*e.g.*, a temporary respiratory overdose which may be of sufficient degree to cause a temporary arrest of respiratory movements; or the undue prolongation of a given degree of CHCl_3 -action beyond its proper period—*i.e.*, the proportion of CHCl_3 is not diminished in accordance with the law of diminishing resistance, and consequently the state of anæsthesia is replaced by relative narcosis.

A variant condition of one of the components of the respiratory machine which is affected

by the negative action of CHCl_3 , or of the blood, which is affected by its physiological action, may not be recognised. If the details of the Graduated Method be not adapted to the requirements of the variant or abnormal condition, the result will be abnormal. And it will be obviously fallacious to explain the production of the abnormal result by some assumed action of CHCl_3 , when it is determined by the condition of the part on which it acts—*e.g.*, the same degree of CHCl_3 -action which is associated with—for there is no evidence as yet adduced in support of the conclusion that it directly causes,—anæsthesia in one individual is associated with narcosis in another. In both the amount of effect produced by CHCl_3 is the same. But the degree of result is different in each, and in the case of narcosis some new phenomena are added. These are due to the negative action of CHCl_3 . Its negative and physiological actions being inseparably associated, the analysis of their respective results will be necessary in order to avoid the error of ascribing the results of negative to physiological action. But the same part may be affected by both actions. The resulting condition of this part will consequently be not simple, but complex.

There is a very general tendency to the production of complex results in the administration of CHCl_3 . And the mistaking a complex for a simple result is the origin of much of the perplexity that follows in the wake of deductive reasoning. For the assumed cause is found to be universally insufficient to explain the result. Thus, because the same degree of CHCl_3 -action is associated with anæsthesia in one condition of the blood and narcosis in another, it is not therefore to be assumed that its physiological action does not remain the same. The misconception concerning that action will be derived from fallacious reasoning. For example: the result, which is to be explained, is directly attributed to CHCl_3 -action. But no demonstrative reason is brought forward to prove a direct relation between them. On the other hand, it is possible that the relation between the "result" and the physiological action of CHCl_3 may be indirect. The effect of CHCl_3 upon the part which it acts upon may produce a direct result which is not apparent, but which becomes an intermediate cause between CHCl_3 -action and the (indirect) result, which is the object under causal investigation. In the case of a complex result, it will be essential to analyse it into its components; and in that of

indirect causation, to isolate the intermediate cause.

A third source of disturbance in the course of CHCl_3 -action is the appearance of a cause which is independent of it. Where two causes are simultaneously in operation, and they exert a direct or indirect influence on the same part, it is necessary to standardise the result upon it of the action of one of them, so as to be able to determine that of the other. In the case of a complication occurring during CHCl_3 -action, this will be effected by, 1, the normal method of inducing anæsthesia; and, 2, the maintenance of the state of normal anæsthesia. The same set of phenomena and the same progressive changes which they undergo are found to be present in the majority of examples. In a small proportion, however, abnormality appears. For example, towards the approach of anæsthesia sudden arrest of respiratory movements occurs. The antecedent phenomena have pursued their normal course. The "arrest" therefore takes place under normal conditions of the respiratory and circulatory system, and of the pupil. And its incidence is observed: it is at the end of expiration. The duration of the phenomenon extends over a period of a few seconds, during which the results of impairment

of the function of aeration, progressively increasing, are manifested. At the end of that period the function of the respiratory centre is spontaneously resumed. This is an instance of the voluntary arrest of the action of the respiratory centre occurring under the most favourable circumstances. Again, in the course of normal anæsthesia there is a sudden manifestation of pallor. It is associated with the disappearance of the pulse. The administration of the CHCl_3 -air atmosphere is discontinued. The displaced base of the tongue is replaced in its normal position so as to assist the declining action of the respiratory machine. After it has reached its lowest limit, the action of the respiratory machine is resumed, and gradually returns to the normal. In the course of this return the pulse becomes perceptible. The strength of the pulse increases in direct proportion to the increasing vigour of the respiratory movements, and eventually reaches the normal, when the administration of CHCl_3 is resumed. These instances of primary arrest of respiratory movements and primary fall of blood-pressure occurring, as they do occasionally during the anæsthetic degree of CHCl_3 -action, can in no wise be ascribed to that action. They do not possess the invariable re-

lationship of antecedent and consequent. And as no cause alters the kind of its effect in the progress of its operation, though its sphere of action may be diverted, it follows that some disturbing factor intervenes to produce the abnormal phenomenon. The causation of occasional phenomena forms, therefore, the subject of inductive investigation. All the possible causes of a given phenomenon are to be isolated. And what the cause of an abnormal phenomenon is in a given example possessing it, is to be determined by inductive reasoning.

The action of a natural cause, as of reflex stimulation of the sympathetic nerve or direct stomachic disturbance, is uninterrupted by the anæsthetic degree of CHCl_3 -action. But not only is it interrupted by the narcotic degree of that action, but its manifestations are also obscured. Thus, a fall of blood-pressure occurring during the state of narcosis as the consequence of reflex stimulation of the vaso-motor centre, is associated with not a decline but a rapid arrest of the action of the respiratory machine. The rate at which the blood returns from the portal to the main circulation is determined by the condition of the lungs. As these are congested the rate will be diminished, and if the degree of congestion be great, the

return of the blood will be temporarily interrupted (during the interval of artificial respiration). Besides, the impediment provided by the obstructed alveolar circulation reacts prejudicially upon the natural recovery of the cardiac function from a condition of reduced action, the consequence of primary fall of blood-pressure, and induced when the right ventricle is distended and the left insufficiently supplied with blood. Thus the results upon the heart and the respiratory machine are complex. There is a degree of pulmonic congestion present when the respiratory centre is sympathetically affected by stimulation of the vaso-motor centre. The abnormal state of the respiratory machine modifies the abnormal action of the centre. The condition of the heart is abnormal at the moment when its function is secondarily reduced, in severe degrees of reflex stimulation of the vaso-motor centre, to a minimum. After it has adapted itself to its new surroundings it begins to recover its function. But the rate of its recovery is gradual and progressive. And thus when the contraction of the right ventricle is of slight range, it will be opposed by increased tension of the pulmonic artery.

This example would tend to introduce error into the study of CHCl_3 -action, unless all the

data which are involved in it are analysed. First, there is the occurrence of a complication during CHCl_3 -narcosis. Secondly, there is the determination of the influence which is exerted by the state of narcosis upon the resultant condition of the heart and respiratory machine. Thirdly, there is the isolation of the component of the state of narcosis—viz., physiological pulmonic congestion, which exerts that influence. And fourthly, the question is presented, What is the relation between pulmonic congestion and the action of CHCl_3 ? Now there is no positive relation between them. Pulmonic congestion is the direct result of the negative action of CHCl_3 . Failure in the analysis of this and other kinds of complex states led to the construction of an unsound hypothesis regarding the physiological action of CHCl_3 . It was assumed to cause positive results which do not belong to it.

§ 79. *CHCl_3 -narcosis.*—The occurrence of examples which resemble, but are not identical with, CHCl_3 -narcosis, renders their exclusion necessary in determining the phenomena of the latter. These examples derive from, 1, mechanical obstruction; or, 2, respiratory overdose which may intervene (a) during the induction of unconsciousness with the normal or

anæsthetic proportion of CHCl_3 , or (b) during the course of normal anæsthesia. They are states, not of simple CHCl_3 -unconsciousness, but of mixed unconsciousness resulting from the temporary intervention of the physical action of CHCl_3 in the abnormal circumstance of respiratory obstruction. Respiratory obstruction produces an altered state of the blood, the proportion of oxygen being diminished, and that of CO_2 increased. This abnormal condition of the blood may be associated with a less than the anæsthetic degree of CHCl_3 -action. But the combined action of respiratory obstruction and CHCl_3 in less than the anæsthetic amount produces an unstable form of unconsciousness. The application of a moderately strong sensory stimulus will in these circumstances be followed by the quick recovery of some degree of consciousness. The result upon the cerebral centres not being a pure CHCl_3 -result, but the suspension of their functions being partially effected by an agency—viz., $-\text{OxY}$ or $+\text{CO}_2$ blood (which is known to be unable to produce a stable form of unconsciousness)—they do not completely withstand the influence of sensory stimuli. Hence the necessity to differentiate between the several degrees of action of these two causal factors when they

are concerned in the production of mixed unconsciousness. The presence of the contracted pupil is an indication that there is no blood-overdose of CHCl_3 . But no other conclusion as to the degree of CHCl_3 -action can be drawn from it, for CHCl_3 may be acting in less than or in the anæsthetic amount. If, however, the pupil is dilated, the indication will be that CHCl_3 is present in narcotic amount; but the degree of narcosis cannot be determined by the degree of dilatation of the pupil while the obstruction remains. For the dilated pupil is a mixed result of, 1, narcotic degree of CHCl_3 -action; and, 2, respiratory obstruction. On the removal of the latter, the pupil will be rapidly reduced to the degree of dilatation corresponding to the degree of narcosis.

The data for the study of the phenomena of the state of CHCl_3 -narcosis are, 1, initial normal conditions of the respiratory machine and the blood; and, 2, the maintenance throughout the course of the experiments of the normal patency of the air-way. The CHCl_3 -air atmosphere is kept as far as is possible constant by the addition of a given measured amount at intervals of 20", so as to prevent the appearance of a temporary respiratory overdose, consequent upon the use of unduly large amounts at longer intervals.

The components of the state of CHCl_3 -narcosis are thus isolated, and are as follows: 1, automatic respiration; 2, increased frequency of respiration, greater than in anæsthesia; 3, increased action of the respiratory machine, associated with impairment of the function of aeration; 4, discoloration of the blood; 5, venous distension; 6, diminution in the frequency and increase in the strength of the cardiac contractions; 7, diminution of muscle-tone, affecting sensori-motor reflex-action; and, 8, dilatation of the pupil, which is less than normally sensitive to the action of light.

Discoloration of the blood, venous distension, and the increased strength combined with diminished frequency of the heart's action, are invariably associated with physiological pulmonic congestion—*i.e.*, distension of the pulmonic artery. There is a cause present and operating to produce obstructed alveolar circulation—*viz.*, the displacement of air in the CHCl_3 -air atmosphere which is breathed. The direct results of this cause are—1, distension of the pulmonic artery, manifested by the diminished frequency and increased strength of the pulse and venous distension of the superficial veins, the former appearing as an early and the latter as a late phenomenon;

and, 2, discoloration of the blood, which is followed by stimulation of the respiratory centre and impaired nutrition of the muscles. Distension of the pulmonic artery and the de-oxygenation of the blood thus become intermediate causes. As their respective degrees of action increase or diminish, so do their results. And as they are both dependent upon the same cause, the variations which they undergo when the degree of its action is varied are in direct proportion to each other. Thus variations of all the indirect results of the cause in question are in the same direct proportion.

It is impossible to produce CHCl_3 -narcosis without at the same time displacing more than the normal proportion of air in the CHCl_3 -air atmosphere. The negative and the physiological actions of CHCl_3 are necessarily combined and their results intermixed. It becomes essential, therefore, to differentiate between them.

All the phenomena, with the exception of the dilatation of the pupil—for in the case of diminished muscle-tone there is a possible cause in the impairment of nutrition, consequent upon an abnormal blood-supply—may be explained by the negative action of CHCl_3 .

The simple displacement of air by means of neutral agents is known not to be associated with immediate dilatation of the pupil, even when the air-way is normally patent. And in the course of the anæsthetic degree of CHCl_3 -action, mechanical obstruction may intervene to produce a considerable degree of duskiess without immediately affecting the condition of the pupil. Again, the dilated pupil, which results from the rapid displacement of air—as, for example, in nearly complete mechanical obstruction—is invariably sensitive. It does not, under these circumstances, gradually dilate. There is an interval during which the degree of duskiess increases while the pupil remains contracted. At the end of that interval it rapidly dilates. On the other hand, in the case of the narcotic degree of CHCl_3 -action, the degree of dilatation of the pupil is directly proportioned to the degree of narcosis present. As the latter increases, the size of the pupil does not rapidly but gradually increase, at the same time becoming less sensitive to the action of light, an attribute which is possessed by no other form of dilated pupil occurring during the administration of CHCl_3 .

The conclusion, therefore, is that the dilated sluggish pupil is either a simple direct or in-

direct result of the physiological action of CHCl_3 . And its isolation leads to the following considerations. I. The simple results of the negative action of CHCl_3 are distension of the pulmonic artery, distension of the right ventricle, increased strength and diminished frequency of the pulse, and venous distension. They are all of them physical results, and can only be produced by a physical cause. II. The simple result of the physiological action of CHCl_3 is dilatation of the pupil. III. The intermixed results of the combined actions are discoloration of the blood, increased frequency of respiration, and diminution of muscle-tone. The investigation will thus become concentrated upon these phenomena.

§ 80. *Different degrees of CHCl_3 -narcosis.*—If the proportion of CHCl_3 be increased, the variation in the CHCl_3 -air atmosphere thus induced will be immediately followed by an increase in the degree of their intensity of all the phenomena of narcosis. The variation in the degree of narcosis is found to be directly proportioned to the variation in the degree of the complex cause. Now the variation in the CHCl_3 -air atmosphere has to be effected gradually in order to obtain uncomplicated results, for the reason that, if too large an increase of

the CHCl_3 -constituent were made, its physical action in the air-way would predominate, and consequently error would be introduced into the results. As the degree of narcotic action is still further increased, the degree of narcosis is also proportionately increased. But there is a limit to the highest degree of narcosis that may be produced without the appearance of an undue degree of intensity of a disturbing factor. For there is a tendency to impairment of nutrition. And this tendency, after a period in which the tissues oppose their resistance to its influence, becomes uncounteracted. Impairment of nutrition leads to impairment of function. And in the case of the ordinary muscles of respiration, the tendency is eventually manifested by the output of less than the normal degree of power.

If the same degree of narcotic action be prolonged beyond a given period, the degree of narcosis tends to increase. The same tendency exists as in the anæsthetic degree, but there is this difference between the two states: in narcosis it appears earlier and progresses with greater intensity.

From the above experimental investigations the following data are derived:—

I. The pupil increases in size as the degree

of narcotic action is made to increase, the variation of the one being directly proportionate to the variation of the other. As the pupil increases in size it becomes less sensitive to the action of light, the variation in the one being in inverse proportion to that of the other. The degree of dilatation may be taken as the measure of the degree of narcotic action on account of its being more accurately determined than changes in the action of the respiratory machine or of the colour of the blood. Any other phenomenon of the state of narcosis might be selected, but variations gradually appearing in the pulse, unless recorded at frequent intervals, or in the colour of the complexion, by reason of its initial abnormality, are not so readily detected, and therefore are not so reliable as the variation in size of the pupil.

II. The frequency of respiration and the discoloration of the blood increase as the degree of narcotic action is made to increase, the variations of the former being directly proportioned to the variations of the latter. Muscle-tone diminishes as the degree of narcotic action increases, the variation of the one being inversely proportioned to that of the other.

The conclusions that are drawn from the study of the different degrees of narcotic action are—I,

that the relation between the cause and the results other than those which are purely negative, with which it is associated, is not of a direct nature. For if those results were due to the action of an agent which produced them by directly affecting—so as to change the condition of—some tissue or nerve-centre, the abnormal condition thus induced, instead of beginning to disappear after the removal of the agent, as is the case with CHCl_3 , would remain stationary for a while—*i.e.*, there would be a period in which the abnormal phenomena preserve the same degree of intensity; 2, that there is a cause—*viz.*, the negative action of CHCl_3 , which is present and operating—which accounts for, either partially or wholly, the set of phenomena comprising accelerated respiratory frequency, discoloration of the blood, and diminution of muscle-tone; and, 3, that the physiological action of CHCl_3 is confined with certainty to the production of changes in the size of the pupil and in the condition of the cerebral centres, and that, seeing it is not yet proved that the negative action produces the whole of respiratory acceleration, discoloration of the blood, and diminished muscle-tone, it is possible that it may be causally related to these phenomena.

§ 81. *The treatment of the state of CHCl_3 -*

narcosis with air.—If at any stage in the course of narcotic action CHCl_3 is discontinued and air alone administered,—the airway being assumed to be normally patent,—an immediate alteration in all the phenomena will be apparent. The respiration becomes less frequent, the blood less discoloured, and the size of the pupil smaller. The degree of narcosis is reduced. And it continues to be still further reduced by the action of air until the normal state of anæsthesia is reached. Just as there is an increase in the intensity of the degree of each individual phenomenon, with an increase of the CHCl_3 -constituent, so there is a diminution when the degree of CHCl_3 -action is reduced. The degree of diminution in the intensity of a phenomenon is determined by the amount by which CHCl_3 is reduced—*i.e.*, by a corresponding increase in the proportion of air. Now the negative action of CHCl_3 is synonymous with impairment of aeration, less than the normal proportion of oxygen being absorbed by the blood. The changes which are at once effected, whether the proportion of CHCl_3 be increased or diminished, are thus explained by a variation in the degree of oxygenation of the blood. But the direct result of $-\text{OXY}$ upon the tissues generally varies in amount according to the nature

of the tissue. The brain, or more accurately that part of it which is the seat of consciousness, and striped muscle-tissue are more sensitive than others to alterations in the proportion of oxygen supplied to them. In normal subjects deoxygenation of the blood, after the removal of its cause, is not followed by a stationary abnormal condition of these tissues. On the contrary, as the proportion of oxygen in the blood tends to become normal, so do the abnormal conditions of the centres of consciousness and the voluntary muscles tend to become normal. Thus these tissues are eventually placed in circumstances which are favourable to the discharge of their respective functions.

Besides exercising this general effect upon the tissues at large, $-\text{OxY}$ or $+\text{CO}_2$ -blood exerts in particular a stimulating influence on the respiratory centre. The degree of stimulation of that centre varies directly as the degree of deoxygenation in CHCl_3 -narcosis within the limit of a given degree of exhaustion of the respiratory muscles. An increase or diminution of the degree of the narcotic action of CHCl_3 is necessarily associated with a greater or less displacement of air in the CHCl_3 -air atmosphere. By virtue of its negative action, CHCl_3 is thus brought into relation with the respiratory centre. But

it is possible that, inasmuch as all the phenomena cannot be explained by its purely negative action, the physiological action of CHCl_3 may have either a direct or indirect influence upon that centre.

The relation of the state of CHCl_3 -narcosis to air brings out two characteristic data which help to isolate the purely physiological action of CHCl_3 .

The period of the return to consciousness varies according to the degree of narcosis; thus the greater the degree the longer the period of time needed for the recovery of the mental functions. But it is essential to exclude the influence of a causal factor which may intervene and affect prejudicially the backward course of the state of narcosis. The causal factor in question is mechanical obstruction in the airway, and it is the consequence of muscular relaxation, which is an indirect result of CHCl_3 -action. The tendency of this factor is to diminish the rate of recovery. If, therefore, the return to consciousness be thus unduly prolonged, the inference might be drawn that the result of CHCl_3 -action upon the cerebral centres is other than what it actually is.

But if comparison be made between the rates of the reoxygenation of the blood in CHCl_3 -

narcosis and in mixed narcosis, resulting from the co-operation of mechanical obstruction and the anæsthetic degree of CHCl_3 -action, the following remarkable difference will be perceived. In the latter the absorption of oxygen takes place with great rapidity, while in the former it proceeds gradually but progressively. Thus, the same degree of blood-change being effected by two different causes, when they are put out of operation the result of the one is dissipated quickly, while that of the other disappears comparatively slowly. The conclusion, therefore, is that there is some factor present in the case of CHCl_3 -narcosis, which tends to retard the oxygenation of the blood. Now CHCl_3 is present in both the above instances—viz., CHCl_3 -narcosis and CHCl_3 -anæsthesia plus mechanical obstruction. But there is a difference with respect to the degree of action in them. This “difference,” therefore, may possibly be associated with the difference in their respective rates of recovery.

The second datum has reference to the proximate cause of the dilatation of the pupil being in the iris. Diminution of muscle-tone is one of the results of the narcotic action of CHCl_3 . The degree of dilatation of the pupil and the degree of discoloration of the blood

are directly proportioned to each other in CHCl_3 -narcosis. But the deoxygenated condition of the blood tends to produce an early result in striped muscles, for the reason that oxygen forms a principal factor in their food-supply. Less than the normal supply of oxygen to them is followed by impairment of their nutrition, and as nutrition and function are intimately related, impairment of the former, after the reserve-power of the tissue is consumed, is followed by impairment of the latter. Under these circumstances, the muscles become less sensitive to the application of ordinary stimuli. They do not respond either with the same readiness or to the same extent as in their normal condition.

The iris, when the pupil is dilated in CHCl_3 -narcosis, presents this characteristic feature of reduced tone. It increases with an increase in the degree of narcotic action. It diminishes with an increase of the volume of oxygen in the blood.

The dilatation of the pupil may thus be the consequence of the diminished tone of the iris. And the diminished tone of the iris is explained by the deoxygenated condition of the blood. But here a difficulty is presented. When oxygen is abstracted from the blood by mechanical

obstruction or by means of a neutral agent, the pupil does not begin to dilate and progressively increase the degree of its dilatation as deoxygenation increases in degree. But it retains its natural condition, even in high degrees of deoxygenation, and dilates only when the action of the respiratory machine becomes interrupted. And when it dilates, it does so rapidly, and at the same time retains its sensitiveness. These conclusions are drawn from results obtained when the abstraction of oxygen is more or less rapid. In CHCl_3 -narcosis, however, the displacement of air in the CHCl_3 -air atmosphere has to be effected gradually in order to avoid a respiratory overdose. And, consequently, through the negative action of CHCl_3 , the reduction of the volume of oxygen in the blood takes place comparatively slowly. There is a difference, therefore, in the length of time over which the same result, produced by different causes, endures. This difference may account for the gradual and progressive diminution of muscle-tone in narcosis. For there is a direct proportion between the degree of the latter and the degree of diminution of the former; and the greater the degree of narcosis, the greater is the reduction of oxygen in the blood. Deoxygenated blood, deriving from the

negative action of CHCl_3 , enters into the causation of reduced muscle-tone. It may or may not be equal to explaining the whole of the reduction. Assuming that the latter is the fact—*i.e.*, diminished muscle-tone is of complex causation—it follows that some other factor is present, and co-operating with $-\text{OXY}$ blood. This factor, then, is either directly or indirectly related to the physiological action of CHCl_3 .

§ 82. *The natural terminations of the progress of the state of narcosis, induced by CHCl_3 .*—Considered in the abstract, increased frequency of respiration is associated with a tendency to the exhaustion of the respiratory muscles. This tendency is manifested by certain changes which appear in the action of the respiratory machine—*viz.*, the range of movements becomes smaller, the undulatory character of the inspiratory movements disappears, and the extraordinary muscles of respiration come into action. If uncounteracted, it eventually results in the arrest of the action of the respiratory machine; the mode of onset of this form of arrest being rapid.

Distension of the pulmonic artery is followed by distension of the right ventricle. The action of the heart is automatically adapted to the increased resistance which is opposed to it.

Its frequency is slowed, while the power of its contraction is increased. If the obstacle remains at the same degree of intensity, the energy of the heart will be progressively diminished as the natural consequence of the increased amount of work which it performs. Thus there is a tendency to the exhaustion of the cardiac power. It will be manifested by the progressive diminution of frequency and the progressive increase of strength of the pulse. And, if uncounteracted, it will eventually result in the disappearance of the latter, the function of the heart being temporarily reduced to its lowest limit under the abnormal circumstances. The mode of disappearance of the pulse is rapid; there is a short interval, during which it becomes thready, and at the end of it no beat is perceptible.

In CHCl_3 -narcosis both these tendencies are present and acting. There is more than the normal amount of work performed by the respiratory muscles; and there is also more work done by the heart than it is ordinarily accustomed to do. If, therefore, arrest of respiratory movements occurs in the course of the investigation of the narcotic action of CHCl_3 in the lower animals, its proper value as a phenomenon associated with CHCl_3 -action

is to be inductively estimated. Thus it is not a primary result, as it would be, if the action of the respiratory centre were directly affected by CHCl_3 . But it is the terminal link in a chain of phenomena attending and rendering abnormal the mechanism of respiration. At the onset of arrest the state of the respiratory machine is abnormal. Its motor-power is temporarily exhausted. To verify the conclusion that muscular exhaustion is the only cause of respiratory arrest, artificial are made to take the place of natural movements of the chest. And after a short interval, in which the distension of the right ventricle is being relieved, and the heart in consequence restored to a condition favourable to the performance of its function—viz., the supply of oxygenated blood to the tissues—the respiratory muscles will resume their work in response to the stimulus of the respiratory centre, the activity of which was prevented from being manifested through their temporary disablement.

The relation between CHCl_3 -action and arrest of respiratory movements or cardiac exhaustion, as being the natural terminations of the state of narcosis, is thus shown to be indirect. And the conclusion that CHCl_3 exerted a specific effect either on the heart or respiratory centre

was drawn, very probably, from the following fundamental error. The same amount of CHCl_3 , administered in the then customary way, is associated with a state which experience proved to be safe. But experience was then limited to cases of comparatively short duration. But if the case were prolonged, owing to the exigencies of the surgical operation, would the introduction of this new element affect the result? The possibility of its doing so having been precluded by the then prevailing notions respecting CHCl_3 -action, the appearance of respiratory arrest or cardiac failure from exhaustion was ascribed, without further question, to its direct influence respectively on the respiratory centre or heart. While, however, the effect of the same amount of CHCl_3 on the part which it acts upon is always the same, the results with which it is associated at different periods of its action are different. The explanation of this difference in results is drawn from the changes which are induced in the conditions of the respiratory machine and blood by the negative action of CHCl_3 . The error, therefore, consisted in leaving out of consideration the influence of those variations, and in deducing the physiological action of CHCl_3 not from a simple but complex result.

An instance illustrating the influence of prolonged duration of narcotic CHCl_3 -action happened in 1883. The subject was a healthy young male adult, and the surgical operation was for the purpose of arresting hæmorrhage from a lacerated wound of large dimensions. A certain quantity of blood was lost during the course of unconsciousness, but it was not supposed to have an influence in determining the time of onset of respiratory arrest. No abnormality was observed to occur in the action of the respiratory machine—the movements being vigorous and accompanied by some noise—until 80' after the beginning of the administration, when it rapidly failed, the pulse at the time being easily felt. The base of the tongue was maintained in its normal position during artificial respiration, which was at once applied. In the course of the treatment the pulse, which at the onset of respiratory arrest presented slow distinct beats, disappeared. Eventually spontaneous respiration was resumed. But it was noticed that the pulse, on the resumption of respiration, was of low tension, and that its strength progressively increased, until it reached what was taken to be its natural character.

In the above instance there was no abnormal

variation in the CHCl_3 -air atmosphere. The physical action of CHCl_3 was restricted to its due limits. And mechanical obstruction, though present in some degree, as manifested by noisy breathing, was proportioned to the degree of muscle-relaxation. The fact that both these causal factors may act independently, the one from an absolute increase in the amount of the CHCl_3 -increment, and the other from displacement of the base of the tongue consequent upon change of position or some local abnormality, as, *e.g.*, abnormal size, tends to complicate the study of the causation of respiratory arrest. Thus rapid or even sudden onset of arrest of the action of the respiratory machine may take place in the early stages of CHCl_3 . But the same phenomena occur in the later stages. In each instance, therefore, it will be necessary, 1, to enumerate all the antecedent phenomena; 2, to record the mode of onset, and all the phenomena appearing subsequently; and, 3, to isolate all the causal factors which are present and acting at the time of its occurrence, in order to arrive at its true causation.

The occurrence of respiratory arrest during the narcotic degree of CHCl_3 -action without any intervening complication, led to a series of experimental investigations which had for

their object the diminution of the proportion of CHCl_3 in the CHCl_3 -air atmosphere administered. Eventually the anæsthetic degree of its action was isolated. But this degree was found to be different for different individuals—*i.e.*, to produce the state of anæsthesia which is known by a set of phenomena which are its invariable concomitants,—a larger proportion is needed for an adult than for a child. In this respect it will be observed that CHCl_3 resembles some drugs—*e.g.*, opium. And further, it was found necessary, in order to maintain the state of anæsthesia during CHCl_3 -action, to progressively diminish its degree. One of the differences between the states of anæsthesia and narcosis is in the condition of the blood. In narcosis it is deoxygenated; the respiratory muscles, consequently, perform the increased work which they have to do under the unfavourable condition of abnormal blood-supply. In anæsthesia it presents the normal colour. The respiratory muscles are supplied with the normal quantity of apparently normal blood. Assuming, however, that the blood is only apparently normal, the degree of change induced in it is obviously less than that in narcosis, and in the circumstances is the least possible. The action of the respiratory machine

should therefore be but little affected, even during long periods of CHCl_3 -anæsthesia—from three to four hours: and this conclusion is verified by experience.

The use of the anæsthetic degree of CHCl_3 -action admits of the accurate study of complicatory causes which operate simultaneously with it, and which may affect either in a like or unlike manner the same parts which are also affected by CHCl_3 . Such a combination of causes is responsible for the vast majority of the so-called states of crises. The part which CHCl_3 plays in their causation is therefore to be isolated. The physiological action of CHCl_3 may be limited to the anæsthetic degree, but owing to a rapid or sudden arrest of the action of the respiratory machine, the presence of CHCl_3 -vapour in the air-way will act as an obstacle in the process of diffusion between the contents of the alveolar region and the atmosphere. Or the respiratory movements may be reduced as the consequence of reflex inhibition of the respiratory centre, and if the proportion of CHCl_3 in the CHCl_3 -air atmosphere be not adapted to the abnormal action of the respiratory machine, a relative respiratory overdose will result. In these instances the action of CHCl_3 is confined to the air-way,

and its results are readily removed either by diffusion or by the artificial expulsion of the contents of the air-way. But CHCl_3 may be acting as a narcotic, and consequently there will be a less or greater degree of distension of the pulmonic artery. Now that abnormality acts as an impediment to the transference of blood from the right to the left side of the heart. If, therefore, a fall of blood-pressure, not of cardiac origin, occurs during narcosis, there will be a delay in the return of the blood from the portal to the main circulation. The source of the delay is mechanical—viz., increased tension in the pulmonic artery. Its degree varies, being directly proportioned to the degree of tension. The action of the respiratory centre being secondarily affected by reflex stimulation of the vaso-motor centre, and stomachic inhibition of the respiratory centre being associated with a corresponding disturbance in the vaso-motor centre, the reduced motor-power of the respiratory machine is confronted with an obstacle in the abnormal condition of the lungs, requiring more than the normal degree of that power in order to overcome partially the resistance which is opposed to it. The action of the respiratory machine will consequently be arrested. And the causation of the arrest will

be complex. First, there is the greater or less degree of pulmonic congestion (*i.e.*, distension of the pulmonic artery), which naturally requires a corresponding increase of respiratory activity, which is effected by an increase in the frequency of respiratory movements, in the absence of a complicatory cause. Secondly, there is the primary or secondary disturbance in the respiratory centre, resulting in reduced action of the respiratory machine. In initial normal conditions of the respiratory and circulatory systems, changes in the one, induced reflexly, are followed by corresponding changes in the other. And when the result on the centre disappears, there is an immediate return to the normal, which is more or less rapidly attained. But if an impediment be in the way of the return to the normal of the action of the respiratory machine, its progress will be checked and it may be interrupted. Such a contingency would necessitate the immediate application of artificial respiration.

In these instances CHCl_3 acts negatively, by inducing pulmonic congestion. CHCl_3 is thus related to respiratory arrest in three different ways: 1, direct physical action in the air-way; 2, exhaustion of the respiratory muscles, an indirect result of its negative and physiological

actions; and, 3, pulmonic congestion, the direct result of its negative action, opposing too powerful a resistance to the reduced action of the respiratory machine consequential upon the intervention of a complicatory cause. The anæsthetic degree of CHCl_3 -action prevents all these possibilities, with the exception of part of the first group, in which its results—viz., respiratory overdose—are relative and readily put out of operation. Besides, it economises the amount of extra work to be done by the respiratory machine, and by preserving the apparently normal condition of the blood, interferes, to the least possible extent, with tissue-nutrition. The following example is therefore of interest, inasmuch as the anæsthetic amount was administered without the appearance of any abnormal phenomena during the period of induction, but with the appearance of a state of crisis in the course of unconsciousness.

The subject was a male infant nine months old, and presented normal characters. Anæsthesia was normally induced by gradually increasing the proportion of CHCl_3 to the maximum, which in this instance was one drop. This is effected by maintaining the amount constant at the maximum, and by gradually dimin-

ishing the open base of the half-cone formed of folded lint: the interval at the end of which CHCl_3 is repeated being determined by the temperature of the atmosphere and the rate of respiration. Soon after the induction of anæsthesia, and while the surgical operation was in progress, the range of respiratory movements became rapidly reduced. For purposes of better observation the child was turned on to its right side; and as a precautionary measure the base of the tongue and lower jaw were drawn forward, so as to ensure a normally patent air-way. The pupil remained contracted, the pulse-beat became stronger and slower, while the degree of duskiness was perceptibly increasing. The respiratory movements remained for an interval of three or four seconds apparently at the same range to which they had been reduced, after which they first exhibited a gradual increase of range, and then rapidly reached the normal. And during their return to the normal duskiness disappeared, being followed by the natural colour of the complexion and the normal character of the pulse.

The course of this complication indicates the presence of a respiratory overdose. In this instance it was an absolute respiratory overdose, as shown by the return of the action of the

respiratory machine to the normal, after the excess of CHCl_3 -vapour in the air-way had been dissipated by the means of diffusion. It was erroneously ascribed to some fault in the method of administration. All traces of the complication having disappeared, the child was again placed in its former position.

But instead of continuing normal as it should do, if no complication is present and the amount of CHCl_3 is progressively diminished, the action of the respiratory machine became accelerated. Displacement of the base of the tongue is a cause of acceleration. The base of the tongue and the lower jaw were drawn forward, and the degree of acceleration was thereby reduced. After an interval of 2' the frequency of the respiratory movements became perceptibly less, and their range diminished. Some degree of duskiness was present, but this was explained by the difficulty experienced in keeping the base of the tongue in its normal position. The pupil was slightly dilated, and the pulse-beats separate, though not, as it was supposed, unduly frequent. The abnormal state presented many features similar to these of direct stomachic disturbance, complicated by either mechanical obstruction or a relative respiratory overdose which had not been early recognised.

But the slight dilatation of the pupil pointed to the presence of another factor which had not as yet been entertained.

Under these circumstances the fold of lint was removed, and the result of air upon respiratory movements, which were becoming still further reduced in range, and were now confined to the abdomen, awaited. This measure is invariably followed, in any case of complication where respiratory movements are present, by an improvement in their movements which gradually increase their range. But instead of any such improvement in the present instance, the abdominal movements became slower, and their range continued to diminish. At this stage the pulse was perceptible, and the pupil was dilated to one-half and sluggish. There was also some degree of venous distension. The pulse disappeared, while the movements of the abdomen continued. And thereupon artificial respiration was at once applied.

The end-object of artificial respiration is to supply air to the alveolar region. In its conduct the nature of the abnormal conditions present and their degrees have to be considered, and the details of the artificial method adapted to their several requirements. Venous distension indicates—1, distension of the right ventricle;

and, 2, distension of the pulmonic artery—*i.e.*, physiological pulmonic congestion. It narrows the calibre of the air-way, and thus retards the rate of diffusion between the contents of the lower air-passages and the outside air. It is impossible to reduce the distension of the pulmonic artery rapidly, for the resistance offered by the chest to its compression admits only of the intake of a small volume of air, the current of which is stayed somewhere in the middle air-passages. An interval of time is therefore needed in order that it may be diffused into the alveolar region, where it is absorbed. Its absorption is followed by the reduction of the degree of tension in the pulmonic artery, and, by consequence, of the degree of pressure in the right ventricle. While the right side of the heart is being relieved from abnormal pressure, the left side is being supplied with a relatively increased amount of oxygenated blood, and consequently the degree of discoloration is diminished.

The base of the tongue and the lower jaw being drawn forward so as to procure the fullest possible degree of patency of the glottis under the abnormal condition of venous distension of the mucous membrane, and the shoulders displaced over the edge of the table so as to favour

the recoil of the chest walls, the lower half of the chest is then gradually but progressively compressed. Difficulty will be encountered by the resistance of the chest walls. It is therefore essential to perform the first compression efficiently, for as much of the contents of the air-way should be expelled as is possible under the circumstances, seeing that the amount of the subsequent intake of air is the same as the quantity of the respiratory contents which are displaced. The act of compression being completed, its cause is quickly removed in order not to impede the recoil of the chest. An interval of 7" was allowed to elapse in the present instance, in order to the diffusion of the air, which occupies the upper and middle parts of the air-way, into the alveolar region, at the end of which the chest was again compressed.

There was no manifest change in the colour of the complexion, or in the size of the pupil (which had become fully dilated). The interval between successive compressions is determined by the degree of resistance offered by the chest. The greater the resistance, the less of the contents of the air-way is expelled; and the less the intake of air, the greater the interval required for the purpose of diffusion.

But after the second compression, and during

the interval, which was reduced to 6", between it and the third, a change became obvious in the coloration of the complexion, and the size of the pupil was perceptibly diminished. Both these phenomena indicate that the air is being uninterruptedly conveyed to the alveoli, where oxygen is absorbed in progressively increasing quantities.

During the third compression, the degree of resistance presented by the chest was felt to be less. And in the interval following it the degree of discoloration of the complexion was still further reduced, and the pupil became smaller.

After an interval of 5" compression was applied for the fourth time. The chest now offered no serious difficulty in the performance of artificial respiration. But this is not a reason for undue haste. The function of aeration subserves the purpose of reducing the pressure in the pulmonic artery. If this abnormal pressure is rapidly removed, there has to be considered the effect which it will have upon the action of the heart. In the present instance the right side of the heart had not been rapidly distended (and even if such had been the case, its rate of reduction is rendered relatively gradual through the intermediation of the state

of apnoea). But the power of the heart has already overcome a greater resistance than is at present opposed to it. It is therefore in a much more favourable position in which to counteract the effect of that resistance when it is progressively and gradually diminishing.

The interval, reduced to 4", following the fourth compression was characterised by a reduction in the degree of distension of the superficial veins. The pupil continued to contract, and the colour of the complexion to improve.

The fifth compression was followed by the disappearance of the last trace of duskiness, and by the normal contracted state of the pupil. And after the appearance of the latter, there was an attempt at spontaneous respiration, in an irregular movement affecting the upper part of the chest. The degree of distension of the superficial veins continued to become diminished.

3" after the fifth, the sixth compression was applied. It was almost immediately followed by abdominal movements,—which were of small range at their commencement, but which were characterised by a progressive increase, not only of range, but also of extent,—the lower thorax first coming into action, and then the middle

and upper. As soon as spontaneous respiration was resumed, venous distension, which had been progressively diminishing in degree, disappeared. But the pulse was not perceptible at the wrist. It was first felt on the appearance of thoracic movements, and thenceforward gradually increased in strength until it reached the normal. The base of the tongue was throughout kept in its normal position until signs of consciousness were manifested, *circ.* 2' after the resumption of spontaneous respiration. And 5' after the recovery of consciousness, the infant was crying in the nurse's arms.

This is an example of gradually induced CHCl_3 -narcosis. The datum that prevented the suggestion of an absolute overdose was the limitation of the amount. But it subsequently transpired that in the course of the administration, and just after the induction of anæsthesia, a quantity of CHCl_3 , *circ.* $\frac{3}{4}$ iii, escaped from the drop-bottle and soaked into the pillow in the immediate neighbourhood of the child's face. The source of the absolute overdose was thus isolated, and the occurrence of, 1, respiratory overdose, due to the rapid, and, 2, blood overdose, due to the gradual, evaporation of the escaped CHCl_3 , explained.

If we compare these two instances of recovery

with artificial respiration, we find that in the former, the degree of CHCl_3 -action, though narcotic, was associated with a long period of increased activity of the respiratory machine; but that in the latter, that period was short, and was followed by manifestations of an excessive degree of obstructed respiration. Thus in the former, the degree of narcotic action was safe within a given period, the length of which is determined by the degree of the initial overdose; but beyond that period it becomes unsafe—*i.e.*, the tendency, inherent in the narcotic action of CHCl_3 , becomes effective when the circumstances are favourable to it. While in the latter, owing to the high degree of the initial overdose, the tendency becomes at once manifested. In the former, respiratory arrest took place before the disappearance of the pulse, but the distension of the right ventricle was very gradually induced. In the latter, however, this distension was induced rapidly. The rate of progress at which the right side of the heart is distended, may have an influence in the determination of the natural but temporary failure in the performance of its function. The question, whether the pulse or the respiration fails first, is therefore not of fundamental importance in

these examples of pure CHCl_3 -narcosis. But inasmuch as the pulse may fail, or the action of the respiratory machine be arrested, as the result of causes severally acting independently of but simultaneously with CHCl_3 , each of these phenomena is of primary importance in its own group. The multiple causation of fall of blood-pressure presents the following analysis:—

I. CHCl_3 being the cause, acting negatively, the disappearance of the pulse is the direct result of cardiac exhaustion, which is indirectly related, through the intermediation of distension of the pulmonic artery, to the negative action of the agent. Its early or late occurrence is determined by the initial degree of overdose, and the length of time over which it operates. The disappearance of the pulse, as the indirect result of the negative action of CHCl_3 , is impossible in the state of anæsthesia, for the reason that its intermediate cause—viz., distention of the pulmonic artery—is absent.

II. The direct cause of the disappearance of the pulse during either anæsthesia or narcosis is reflex stimulation of the vaso-motor centre. The vaso-motor centre may be reflexly stimulated, either early or late, in the course of CHCl_3 -unconsciousness. In the case of anæs-

thesia, the complication runs its natural course without any opposition. But in the case of narcosis, the progress of the complication is interrupted, and what is, in normal conditions, a temporary disappearance of the pulse, becomes a relatively permanent one when the return of the blood from the portal to the main circulation is delayed at the alveoli. But it ceases to be permanent when the factor upon which permanence depends—viz., alveolar obstruction—is removed by artificial respiration.

It is this group of examples,—fall of blood-pressure deriving from reflex stimulation of the vaso-motor centre, associated with some degree of obstructed respiration,—in which the pulse disappears before the respiration fails, that gave support to the opinion that CHCl_3 acts directly upon the heart. And it is to this group that the vast majority of instances of fall of blood-pressure belong. And the reason why they present a greater element of danger than simple cases of CHCl_3 -narcosis is that they are associated with alterations in the states of the circulatory and respiratory systems that are suddenly or rapidly induced, whereas, in the latter, these changes are induced more or less gradually.

§ 83. *CHCl_3 or product of decomposition circulating in blood.*—The opinion that CHCl_3

affects directly either the respiratory centre or the heart, presupposes its presence in the blood. It is absorbed into the blood, and carried by the circulation to those parts. But the actual presence of CHCl_3 in the blood has as yet not been demonstrated. It possesses a characteristic odour, but not the slightest trace of it is recognised in blood issuing from a wound during CHCl_3 -unconsciousness, either in anæsthesia, where the blood is apparently normal, so far as colour is concerned, or in narcosis, where the blood is dark; the explanation of discoloration being, for the present, given to negative action.

There is a presumption, therefore, that CHCl_3 does not exist in the blood. Assuming that it does not, it will undergo some change either in the way of decomposition or entering into a higher combination. The CHCl_3 -product will thus be the cause of respiratory arrest or cardiac depression. But the same difficulty surrounds its identification in the blood, as affects CHCl_3 itself. It eludes all attempts at isolation. Nothing can positively be ascertained concerning it from the examination of the blood or urine.

If CHCl_3 does not exist in the blood, what evidence is there that its product is the direct

cause of cardiac weakness? The disappearance of the pulse. But does the disappearance of the pulse necessarily originate in the heart? No, for it is also the direct result of reflex stimulation of the vaso-motor centre, the accompanying reduced action of the heart being indirectly produced. If, however, it does originate in the heart, is it necessarily associated with weakness, such as is directly caused by the action of a cardiac depressant? No, for temporary exhaustion results from overwork, which means the consumption of more than the normal amount of energy. If, lastly, it does originate in cardiac weakness, is the heart necessarily depressed by the direct effect of the CHCl_3 -product? No, for the heart is in some cases initially abnormal, and its function liable to fail at a moment which cannot be determined. The argument drawn from the disappearance of the pulse, even supposing the CHCl_3 -product to be present, and assumed to be effective, is thus inconclusive. For, 1, the pulse may temporarily disappear without any primary change in the action of the heart; 2, the pulse may temporarily disappear as the consequence of a change in the condition of the right side of the heart, indirectly caused by alveolar obstruction.

§ 84. *Direct and indirect action : remote results.*

— CHCl_3 -action is associated with the state of unconsciousness. The natural state of unconsciousness is composed of, 1, automatic respiration; 2, the contracted pupil; and, 3, muscle-relaxation, and is consequent upon the suspension of the functions of the cerebral centres. In the case of CHCl_3 , there are different degrees of result upon the cerebral centres according to the degree of its action. This follows from the difference in the time required for the recovery of their functions. Thus, in anæsthesia, the interval between unconsciousness and consciousness is relatively short; in narcosis it is relatively long, its length being directly proportioned to the degree of narcosis.

The phenomena are not the same in anæsthesia and narcosis. The pupil is dilated and sluggish, and muscle-tone is diminished in the latter, whereas, in the former, the pupil is contracted, and there is at its commencement no perceptible change in muscle-sensitiveness. But in the course of anæsthesia, the tendency to become less sensitive to the influence of a local stimulus appears.

The question then arises, are these differences—viz., dilatation of the pupil and diminished

muscle-tone—dependent upon a higher degree of result on the cerebral centres, associated with the purely physiological action of CHCl_3 ? For its negative action certainly does not cause indirectly the sluggish, dilated pupil, and probably is not the chief factor in the causation of diminished muscle-tone.

Now, in the case of the pupil, there is no one condition of it which is the invariable concomitant of all states of unconsciousness, however they may be produced. Thus natural sleep is associated with the contracted pupil; so is opium-narcosis, and CHCl_3 -anæsthesia, while in CHCl_3 -narcosis and alcohol poisoning it is dilated. The same want of uniformity is also obvious when the cause is pathological. Unconsciousness resulting from hæmorrhage may be associated with either a dilated or contracted pupil. The inference, therefore, is that there is no intimate relationship between the condition of the cerebral centres and that of the pupil, and the size of the pupil will thus be determined by a causal factor which is directly related to it. Such a causal factor may appear as the intermediate result of the primary cause. It may exist as a tendency, the effect of which is counteracted by the influence of certain conditions, and becomes

manifested when these begin to offer less resistance to its action.

There is some ground for the assumption that the relationship between CHCl_3 -action and the pupil is of a more intimate nature than that of secondary causation. The variations in size which it undergoes are directly proportionate to variations of the degree of CHCl_3 -narcosis. There are, then, three phenomena which are invariably associated with the state of narcosis—viz., the dilatation of the pupil, diminution of muscle-tone, and the abnormal condition of the centres of consciousness. And these form the foundation of the inductive investigation of the physiological action of CHCl_3 . Each undergoes a degree of variation which is directly proportioned to the degree of variation of the narcotic action of CHCl_3 . Their several variations, therefore, in any one example, are directly proportioned to each other. The dilatation of the pupil may be partly or wholly due to diminution of muscle-tone. As the size of the pupil increases, the sensitiveness of the iris diminishes in an inverse proportion. Assuming that diminution of muscle-tone is the sole factor in the causation of dilatation, variations in the size of the pupil would consequently become “accidental” phenomena, and thus

subserve the purpose of indicating the characteristic change affecting the iris—viz., diminished muscle-tone.

What, then, is the relationship between the abnormal condition of the cerebral centres and diminished muscle-tone? Are they both the indirect results of the same primary cause, or do they possess a direct causal relationship? In the latter contingency, the "antecedent" will be the abnormal condition of the cerebral centres, and the "consequent," the abnormal condition of the striped muscles, inferred from the impairment of their function. But is it the fact that the abnormal condition of the centres of consciousness, when it varies in degree, is invariably followed by a corresponding degree of impairment of muscular function? No, for the relationship between those centres and the voluntary muscular system is not a direct one, but they are connected through intermediate co-ordinating centres. The voluntary muscles are thus subject to the direct influence of these lower centres, and also to variations, both of quantity and quality, of the blood supplied to them.

Diminished muscle-tone and the abnormal condition of the cerebral centres are therefore collateral results of CHCl_3 -action. Now, CHCl_3 ,

in its physiological sphere of action, can only have one effect. The part upon which this effect is produced cannot be the seat of consciousness, for the simple reason that different degrees of the abnormal condition of the cerebral centres do not explain the different degrees of diminished muscle-tone. Nor can it be the voluntary muscular system, for primary muscle-changes are known to be in no wise related to changes in the cerebral centres.

As neither diminished muscle-tone nor the abnormal condition of the cerebral centres can be proved to be a direct result, it follows that they are both indirect results of CHCl_3 -action. They have, therefore, a common cause, which is the direct result of the physiological action of CHCl_3 . Variations in the degree of CHCl_3 -action are followed by corresponding variations in the degree of action of its intermediate cause. And variations in the latter will explain the direct proportion which exists between the accompanying variations in degree, both of the abnormal condition of the cerebral centres and of diminished muscle-tone.

The action of a cause is immediately followed by its effect, which becomes manifested in the resulting change of the condition of the part affected. This is the primary or fundamental

phenomenon. But when the part primarily affected is intimately connected with another part, or parts, the changes induced in the former are followed by corresponding changes in the latter. And these also become manifested in their several results. In the course of CHCl_3 -action, many phenomena appear simultaneously or in succession. The fundamental phenomenon is the first to appear, and is followed by other phenomena which are called indirect, because their connection with the action of the primary cause is not so intimate as that of the former. But in the case of CHCl_3 , a very considerable difficulty is presented at the outset by its multiple action. For the first phenomenon to appear is acceleration of the respiration. The administration of CHCl_3 is associated with the displacement of air. A reduction of the normal amount of air is, under these circumstances, followed by increased frequency of respiration. There is a cause, present and in operation, other than the physiological action of CHCl_3 , to explain the stimulation of the respiratory centre. It is associated with the negative action of CHCl_3 . Consequently, the isolation of the fundamental phenomenon of the physiological action of CHCl_3 is obscured.

The difficulty in determining the part which is primarily affected by CHCl_3 , acting physiologically, may therefore be the source of erroneous conclusions drawn from the results of experiments. For it is conceivable that while the amount of CHCl_3 is made to vary in the CHCl_3 -air atmosphere, the condition of the part may be different in different examples—in some being normal, and in others presenting not only different kinds of abnormality but also different degrees of the same abnormality. In these circumstances, sound conclusions are impossible, for the reason that the influence of a disturbing factor—viz., the condition of the part affected is not taken into consideration. When the degree of action of a cause is constant, and the condition of the part it affects is the same in different examples, the results will be uniform. If the degree of action is normal and the condition of the part normal, then the results will be normal. But in the case of CHCl_3 , the same degree of action is not in all examples attended by uniformity in results. To arrive at uniformity it is necessary to classify the examples according as they present—1, differences in quantity, and, 2, differences in quality of the blood. Thus, the same amount of CHCl_3 is required for the induction of anæsthesia,

when the amount of blood is the same. When this amount is less, then less CHCl_3 will be needed to induce anæsthesia—*i.e.*, a less degree of CHCl_3 -action will be required. So in anæmia, the greater its degree, the less the amount of CHCl_3 necessary to induce anæsthesia. These data point to a direct relation between CHCl_3 and the blood. But before such a relation can be admitted it is necessary to exclude the influence of the negative action of CHCl_3 . There is a displacement of air in the atmosphere breathed, and consequently a reduction of the volume of oxygen in the blood, during the administration of CHCl_3 . The reduction of oxygen in the blood is known to be followed by comparatively greater results in the anæmic than in the normal. The negative action of CHCl_3 will thus provide a reason for the difference in the amounts of CHCl_3 which they respectively require.

In regard to the intermediate cause, which is the result of CHCl_3 -action, the following have to be considered: 1, the phenomena of CHCl_3 -action are evanescent—*i.e.*, in order to their maintenance, it is necessary to continue the administration of CHCl_3 . This fact is demonstrated by means of the normal method—*viz.*, the use of the anæsthetic quantity at

short intervals; and, 2, CHCl_3 is destroyed, and therefore its dependent cause ceases to operate, and its results disappear. These results begin to disappear immediately after the withdrawal of CHCl_3 . It follows, therefore, that the connection between the intermediate cause and its results is a very sensitive one. And as there is no trace of any enduring abnormal result after the return to consciousness, it also follows that the part which is primarily affected by CHCl_3 , the abnormal condition of which is responsible for the phenomena of its physiological action, recovers its normal condition.

§ 85. *Relation of CHCl_3 to the phenomena appearing in the course of its action.*—It is necessary, therefore, to inquire into the relation which exists between the physiological action of CHCl_3 and each individual phenomenon which accompanies it; and to explain its manner of causation, not by assuming one particular causal factor, but by the enumeration of all the possible factors, and the successive exclusion of those which are unequal to account for the facts. Thus, the blood is discoloured in narcosis, but in anæsthesia there is no change of colour that can be detected by the naked eye. In narcosis, the negative action of CHCl_3 explains the dark colour of the blood. It might

be thence inferred that the physiological action of CHCl_3 has no influence on the colour of the blood. But before a universal conclusion can be reached, all the data entering into it have to be considered. One of these is the difference in the degree of CHCl_3 -action. Now, experience proves that the conclusion is true when the degree of CHCl_3 -action is limited to the anæsthetic. In CHCl_3 -narcosis, however, there are two factors, one being the negative, the other the narcotic, action of CHCl_3 . It is possible, therefore, that the narcotic action of CHCl_3 may cause to some extent the discoloration of the blood. It does not necessarily follow that because one degree of CHCl_3 -action is not associated with dark blood a different degree is also unaccompanied by this abnormal condition. Proof, therefore, is to be adduced that the physiological action of CHCl_3 , in narcotic degree, does not discolour the blood before the conclusion becomes universal that CHCl_3 produces no alteration in the colour of the blood.

It is just this proof that is so difficult to obtain by the ordinary means of administration. For with each increase in the proportion of CHCl_3 in the CHCl_3 -air atmosphere, there is a corresponding diminution in the volume of

air. Thus, as the degree of narcosis increases, so does the discoloration of the blood; but at the same time negative action increases—*i.e.*, the proportion of air diminishes. The means of obtaining this proof are therefore to be sought indirectly. And here the comparative study of different kinds of narcosis in their relation to air leads to the acquisition of an important datum. Narcosis is induced by mechanical means up to a given degree, which is measured by the degree of discoloration of the blood. When the obstruction is completely removed, reoxygenation of the blood rapidly takes place, and its normal colour is restored within 3" or 4". If the same degree of discoloration of the blood be produced by a CHCl_3 -air atmosphere, the air-way being supposed to be normally patent, and the mixed atmosphere changed for air, reoxygenation of the blood will immediately begin, but it will proceed more slowly, so that the normal colour of the blood will not be restored until after an interval of 30". What is the explanation of the difference in the length of the periods required by these states respectively for their return to the normal? Apparently it resides in some factor which retards the process of oxygenation in CHCl_3 -narcosis. This factor, then, has some

relationship to CHCl_3 -action, for the above examples are alike in all respects but one—*i.e.*, CHCl_3 is acting in one of them but not in the other.

It will be obvious, therefore, that this datum supplies a means for the isolation of the physiological action of CHCl_3 . The possible inferences are—1, CHCl_3 interferes with the process of oxygenation, through its influence on the coloured blood-corpuscles; 2, the presence of a CHCl_3 -product in the blood tends to prevent the absorption of oxygen; and, 3, CHCl_3 itself is oxygenated by, and consequently abstracts oxygen from, the blood.

But further data are needed in order to prove or disprove any of these possible solutions. And these data will appear in the following series of investigations.

§ 86. *Relation of CHCl_3 to the cerebral centres.*
—The cerebral centres are more sensitive to changes in the volume of oxygen in the blood than the spinal centres or nerves. One of the reasons for this is their relatively large blood-supply. Another one is their extremely delicate structure. A certain degree of reduction in the volume of oxygen affects their nutrition, therefore, so far as oxygen is concerned, in greater degree than that of less vascular tissues.

Change in nutrition is synonymous with change in function. Thus it follows that the functions of the cerebral centres may be suspended without any undue interference with the functions of other centres and tissues, by reducing the proportion of oxygen in the blood to a given percentage; and also that the suspended function is not associated with any change in the condition of the centres themselves, other than that following upon a shortage of oxygen. When the volume of oxygen is restored to the normal, the conditions for normal nutrition are restored, and therefore function returns—*i.e.*, consciousness. And if function quickly returns to the normal, it is proof that the abnormal effect upon the cerebral centres is evanescent. But suppose the proportion of oxygen to be reduced below that which is actually sufficient for the production of unconsciousness, the result upon the cerebral centres will be an increase in the impairment of their nutrition. And if the abnormal degree of minus oxygenation be prolonged, the tendency, which is at first counteracted by the reserve power of the centres, to the progressive diminution of their vitality will appear. A longer interval will thus be necessary for their normal oxygenation, and its length will be determined by the degree of

deoxygenation and the period over which it extends. But though the return to consciousness in these abnormal circumstances will be prolonged, yet no permanent change is induced in the condition of the cerebral centres. For as soon as they become normally oxygenated, their functions will be normally restored.

There is then a difference of degree in the minus oxygenation of the cerebral centres. And the different degrees will be represented by different degrees of the state of unconsciousness. The lowest degree of unconsciousness is termed anæsthesia, and the higher degrees are called generally states of narcosis, the particular degree of any one of them being determined by the degree of discoloration of the blood. In the case of CHCl_3 , the size of the pupil varies directly with the fundamental phenomenon—viz., discoloration of the blood. It is taken to be the measure of the degree of CHCl_3 -narcosis, for the reason that delicate variations in its size are more accurately estimated than slight alterations in the colour of the blood.

The phenomena of the different degrees of the physiological action of CHCl_3 are accompanied and sometimes complicated by the results of its negative action. In anæsthesia, these are reduced to a minimum. But in

narcosis, negative action is not completely counteracted. And thus collateral phenomena appear in, 1, the abnormal character of the respiratory movements; and, 2, discoloration of the blood. In these circumstances, the physiological results tend to be obscured. It is conceivable, and therefore possible, that both the negative and physiological actions of CHCl_3 are related to the same part. The resulting phenomena consequential upon this combined action will therefore be, on the supposition that they are so, complex. And therefore it will become necessary to analyse each complex phenomenon with its component parts, and to ascribe each of them to its proper source in negative or physiological action.

The maximum proportion of CHCl_3 in the CHCl_3 -air atmosphere needed for the induction of anæsthesia by the graduated method varies according to the quantity and quality of the blood. The suspension of the functions of the cerebral centres is not (and cannot be, by this means) effected immediately,—for the reason that there is a transitional period between consciousness and unconsciousness, which is shorter with the rapid, longer with the graduated method. During it, the will may be influenced by emotion, and manifest itself either

by inhibition of the breathing or muscular movements, or both. The degree of emotion may also become intensified. In these abnormal circumstances, it will be necessary to regulate the CHCl_3 -air atmosphere to the actual degree of action of the respiratory machine, on the principle that a given CHCl_3 -air atmosphere, which is normal for the normal action of the respiratory machine, becomes relatively abnormal when respiration becomes abnormal.

In the course of the induction of anæsthesia, external consciousness first disappears, and is followed after an interval by the suspension of the purely mental functions. The last of these to disappear is the will. And the last act of the will may be arrest of the respiratory movements. Voluntary arrest of the function of the respiratory centre may occur at any stage in the course of the induction of unconsciousness. It is always necessary, therefore, in view of this possibility, to preserve the different components of the respiratory machine in their natural condition.

The use of the anæsthetic proportion of CHCl_3 in the CHCl_3 -air atmosphere, continued at regulated intervals, counteracts in normal examples the tendency to its physical action. The action of the agent, CHCl_3 , is thus made,

as far as is possible, constant. The advantage of this constant action is evident in the facility with which the operation of an intervening cause is studied. But in order to maintain the state of anæsthesia, the proportion of CHCl_3 in the CHCl_3 -air atmosphere has to be progressively diminished, in accordance with the law of diminishing resistance. The abnormal condition of the cerebral centres, associated with the complete suspension of their functions, being maintained by a relatively less degree of CHCl_3 -action, it follows that the centres undergo some change, which renders them more sensitive to the influence of CHCl_3 . Now, there is evidence that, in the course of anæsthesia, they receive less than the normal supply of oxygen. But a small degree of shortage in this respect is not immediately followed by a change in the condition of the cerebral centres. Like other tissues, they oppose more or less resistance to alteration in their nutritional surroundings, and thus tend to preserve a state of equilibrium. But their power of resistance, which is expressed in the actual degree of their vitality, is thereby reduced, and in order to restore it to its normal capacity again oxygen is needed. If, therefore, the disturbing factor—viz., shortage of

oxygen — is not removed after the interval, during which its encroachment upon their vitality has been successfully resisted, its tendency becomes effective in the less degree of resistance which is opposed to it. And the degree of resistance will be progressively diminished if the shortage of oxygen remains the same; but maintained at its highest possible under the abnormal circumstances, if the proportion of oxygen is progressively increased. This change in the condition of the cerebral centres, induced by the prolonged action of CHCl_3 , is the foundation of the law of diminishing resistance. They become more sensitive to the influence of CHCl_3 in the course of its action, and therefore, in order to produce the same result in them, less of the agent is needed.

The same degree of CHCl_3 -action, if prolonged, will be followed by an increase in the degree of results. Thus, the same proportion of CHCl_3 in the CHCl_3 -air atmosphere is "anæsthetic" for the first, "narcotic" for the subsequent periods of unconsciousness. And CHCl_3 -narcosis implies impairment of the function of aeration. Now, the same degree of CHCl_3 -action being associated with the normal colour of the blood and the contracted

pupil at an early stage, and with discoloration of the blood and dilatation of the pupil at a later, the question arises, what is the cause of the difference in results? Change in the condition of the cerebral centres cannot explain the occurrence of these phenomena. Their causation, therefore, is to be sought elsewhere. And there is the following indication of its origin. For the same CHCl_3 -air atmosphere is not invariably associated with the state of narcosis: it becomes so only when the circumstances are favourable. The circumstances point to the physical action of CHCl_3 . The CHCl_3 -air atmosphere, after a while, is not efficiently expelled by the action of the respiratory machine. Consequently, the power of the latter undergoes some degree of reduction. The explanation of the occurrence of the phenomena of narcosis in the course of the continued initial anæsthetic degree of CHCl_3 -action is thus traced to a reduction of the power of the respiratory machine.

The relation between CHCl_3 -action and the set of phenomena, comprising automatic respiration, muscle-relaxation, and the contracted pupil, is thus defined. They are the concomitants of the suspended functions of the cerebral centres. In the state of uncon-

sciousness, the connection between the cerebral centres and the respiratory centre is temporarily interrupted; and, consequently, the latter assumes its natural action. So, in the case of the voluntary muscles, they are temporarily disconnected from the centres of volition; and, consequently, they assume their natural condition. But their connection with the spinal centres is not affected by the suspension of the functions of the cerebral. Reflex stimulation will therefore, on the supposition that no dependent or independent condition intervenes and prevents it, be followed by movement. In the case of the pupil, its natural state, so far as regards the simple suspension of the cerebral functions, is the contracted. But its size may be affected in a positive way by the action of CHCl_3 .

These phenomena, therefore, with the exception of the sluggish pupil, are but secondarily related to CHCl_3 -action. CHCl_3 suspends either directly or indirectly, and the evidence is in favour of the latter means, the function of the cerebral centres. And the contracted pupil, muscle relaxation, and automatic respiration appear as the natural consequences of the interrupted relation between the pupil, voluntary muscles, and the respiratory centre on the one

hand, and the suspended functions of the cerebral centres on the other. But the pupil is dilated, and the muscles are less sensitive to the influence of direct stimulation, in CHCl_3 -narcosis. These facts supply evidence of the presence of a causal factor, which is independent of the suspended functions of the cerebral centres. Thus, a causal factor dependent on CHCl_3 -action suspends the cerebral functions, and causes secondarily muscle-relaxation. But in CHCl_3 -narcosis, a causal factor also dependent on CHCl_3 produces loss of muscle-tone. It is probable, therefore, that these causal factors are identical. Thus, the action of CHCl_3 causes on supposition deoxygenation of the blood, and deoxygenated blood (1) suspends the functions of the cerebral centres, and is accompanied by simple muscle-relaxation when the degree of its intensity is limited to anæsthesia, and (2) causes loss of muscle-tone when present in a higher degree of intensity.

The subsidiary conclusions derived from the investigation of the relation between CHCl_3 and the cerebral centres are the following: I. There is a source of deoxygenation of the blood in the negative action of CHCl_3 . This is actually evidenced in narcosis. There is retardation in the oxygenation of the blood in

narcosis. The oxygen supply to the cerebral centres is gradually restored to the normal, and coincides with the gradual return of the cerebral functions. There is no permanent disturbance induced in the condition of the cerebral centres—*i.e.*, as soon as the action of CHCl_3 is made to cease the cerebral centres do not remain in the same abnormal condition which they are in before its removal, but immediately begin to recover their functions. The progress of their recovery may be delayed by the influence of a collateral cause—*viz.*, the displacement backwards of the base of the tongue—which operates by diminishing the supply of air to the alveoli, and consequently retarding the normal oxygenation of the blood. II. There is no actual evidence of a reduction in the volume of oxygen in the blood in anæsthesia. The amount of air displaced by the vapour of CHCl_3 in this degree of its action does not suffice to explain the suspension of the function of the cerebral centres; for a higher degree of deoxygenation than it produces is needed for that purpose. The colour of the blood is apparently normal in anæsthesia, while it is dark in narcosis. On the supposition that there is less than the normal volume of oxygen in the blood in anæsthesia, it follows, 1, that there

are some degrees of its deoxygenation which are not associated with its discoloration; and, 2, that if $+\text{CO}_2$ is the cause of discoloration, a diminution of the volume of oxygen may be present without a corresponding increase of the volume of the former.

On the assumption that CHCl_3 exercises a direct influence on the cerebral centres, where the condition of these varies from the normal, as in delirium tremens, hydrophobia, the status epilepticus, and in the insane, it should tend to introduce abnormality in the result. Thus, the anæsthetic amount for a normal case would be narcotic for one that presented cerebral centres opposing less than the normal resistance to the action of CHCl_3 , and insufficient to produce anæsthesia in another whose cerebral centres opposed a greater resistance than the normal. But no such abnormality universally occurs. When it does occur, it is invariably accompanied by some variation from the normal either of the quantity or quality of the blood. For example, in the status epilepticus a less degree of CHCl_3 -action than the anæsthetic is needed to induce unconsciousness, not because the cerebral centres are primarily abnormal, but because the quality of the blood is abnormal. There is invariably some degree of deoxygena-

tion of it. And experience shows that in that condition of the blood, without any exception and however it may be produced, less than the normal amount of CHCl_3 suffices to induce unconsciousness, the actual amount in any particular case being determined by the degree of deoxygenation which is present.

The relationship between deoxygenation and unconsciousness may be drawn from experiments with a neutral — OXy-atmosphere. Such an atmosphere is provided by nitrous-oxide gas, which temporarily takes the place of oxygen, forming a weak combination with hæmoglobin. But the degree of deoxygenation necessary to produce unconsciousness cannot by this means be reached without considerable impairment of the function of respiration. For it induces distension of the pulmonic artery; and distension of the pulmonic artery leads to distension of the right side of the heart, and, remotely, to general venous distension. The duration of unconsciousness induced by nitrous-oxide gas is thus necessarily short. A certain degree of deoxygenation being a cause of the suspension of the functions of the cerebral centres, it is conceivable that it may be effected by another means than that of diminishing the proportion of oxygen in the atmosphere which is respired,

or even of its complete withdrawal—viz., by the abstraction of oxygen by an agent circulating in the blood. The seat of deoxygenation would thus be transferred from the alveoli, where it is necessarily associated with impairment of the functions of respiration and aeration, to the blood itself, in which deoxygenation may take place without any impairment of these functions, provided that the introduction of the agent, which is effected by respiration, is not accompanied with impairment of aeration. And, further, the action of the agent can, on the supposition, be limited to the necessary degree of deoxygenation. And as the phenomenon accompanying any degree of unconsciousness, and determining it—viz., automatic respiration—does not determine its degree, and as it is essential to use the lowest degree of unconsciousness, the knowledge of the phenomena which characterise that degree—viz., normal colour of the blood and the contracted pupil—will lead to the limitation of the action of CHCl_3 to its lowest or anæsthetic degree.

§ 87. *The relation of CHCl_3 to the respiratory centre.*—The first phenomenon appearing in the course of the action of CHCl_3 , in the absence of complications, is increased frequency of the respiration. The frequency gradually increases

in direct proportion to the gradual increase of the degree of CHCl_3 -action, until it reaches the maximum of 28, at the onset of normal anæsthesia. In the progress of the state of anæsthesia, which is effected by a progressive diminution of the degree of CHCl_3 -action, increased respiratory frequency presents two stages. The first is characterised by its stability, and extends over a period of 30' in normal examples—a less degree of CHCl_3 -action being thus associated with the same degree of frequency of the respiration. In the second there appears an additional increase in the frequency, which has an interval of relative stability, and afterwards is followed by a further increase in its degree: thus a diminishing degree of CHCl_3 -action is associated with an increasing degree of respiratory frequency.

Volition successfully counteracts this influence of CHCl_3 -action. In the case of the lower degrees of the emotional state, the initial increased frequency of respiration is affected in the same way as in the normal—*i.e.*, its degree is gradually raised until the onset of automatic respiration. But the maximum frequency in any particular instance is not a pure result, for the reason that the secondary influence of emotion on the respiratory centre does not

cease immediately when anæsthesia is induced. A period of 3', during which all traces of emotional results disappear, is therefore allowed to elapse before the frequency of respiration is taken, in order to obtain a CHCl_3 -record free from complication. In the case of initial acceleration of the respiration—fever, pneumonia—which is relatively permanent to the period of CHCl_3 -action, the same variations are manifested as in a normal example. But the respiratory frequency is never in any one instance a simple CHCl_3 -product, for the reason that a cause of respiratory frequency, acting independently of, and simultaneously with, CHCl_3 , is always present.

Increased frequency of respiration is the consequence of stimulation of the respiratory centre. There is a known cause of stimulation, provided by the negative action of CHCl_3 , in the diminution of the volume of oxygen or increase in that of CO_2 in the blood. The degree of stimulation determines the degree of respiratory frequency. Hence, as the negative action increases—*i.e.*, there is a smaller proportion of air in the CHCl_3 -air atmosphere—the degree of the stimulus will be increased (the air-way being supposed to be always normally patent). Respiratory frequency, therefore, will

be greater in narcosis than in anæsthesia. And as there are different degrees of narcosis, it will be relatively greater in the higher than in the lower ones. On the withdrawal of CHCl_3 respiratory frequency is at once reduced, and continues to undergo a rapid reduction until it reaches the normal at the end of an interval of *circ.* 5'. These phenomena invariably accompany the induction, maintenance, and termination of the state of anæsthesia. They form, therefore, the foundation on which the relation of CHCl_3 to the respiratory centre is to be based. But occasionally other phenomena present themselves in the action of the respiratory machine during CHCl_3 -unconsciousness. And it is these occasional phenomena that gave rise to the view that the action of CHCl_3 is peculiar.

Thus, in the course of anæsthesia, the action of the respiratory machine may become reduced both in range and frequency. It is the consequence of the inhibited action of the respiratory centre. There are but two causes known to inhibit the function of this centre. The one is volition, and is excluded by reason of its temporary suspension; the other is associated with the occurrence of abnormality in the function of the stomach, interruption to the

progress of digestion being followed by stimulation of the terminals of the vagus, leading to reflex inhibition of the action of the respiratory centre. If, in these circumstances, the proportion of CHCl_3 is regulated according to the actual degree of the reduced action of the respiratory machine, anæsthesia may be maintained during the temporary abnormal condition of the respiratory centre. And on the removal of the reflex stimulus, coinciding with the expulsion of the stomachic contents, the action of the respiratory centre immediately returns to the normal, and is manifested by the reappearance of the normal action of the respiratory machine. There is nothing to indicate the approach of stomachic inhibition of the respiratory centre, and the period of its duration varies. It is necessary, however, to raise the proportion of CHCl_3 to the normal, in order to maintain anæsthesia, when the action of the respiratory machine becomes normal—*i.e.*, to what it would be had no intercurrent phenomenon appeared. If, therefore, the action of CHCl_3 , in the example just given, be assumed to be direct on the respiratory centre, the hypothesis is confronted with the following difficulty. CHCl_3 -action is invariably accompanied by increased frequency of respiration

when all complications are absent. But when a particular complication is present, the action of the respiratory machine is reduced not only in frequency but also in range, even though CHCl_3 continues to act. What is the origin of the complication? If it be assumed that it is CHCl_3 , the manner of its procedure in inducing a reduction in the power of the respiratory machine is yet to be explained. Now, there is no evidence of its physical action in the air-way, for there is no duskiess. The seat of its influence, therefore, cannot be placed in the air-way. And if not in the air-way, it follows as a necessary consequence that it cannot be in the lungs. The source of the reduced action of the respiratory machine being demonstrated not to be in any one of its components, it follows that it derives from some abnormal condition of the respiratory centre. Thus CHCl_3 in a few exceptional instances causes on assumption inhibition of the function of the respiratory centre; but in the generality of cases it is associated with its stimulation. These two results on the action of the respiratory centre are directly opposed to each other. But the physiological effect of CHCl_3 on the respiratory centre is, and can only be, one and the same. The argument ascribes to

it either an inhibitory or stimulant influence. But the difficulty is overcome by ascribing the origin of the complication to its proper cause, which, in this group, is independent of, but operates simultaneously with, CHCl_3 .

Arrest of respiratory movements is another phenomenon which may, and does occasionally, occur in the course of CHCl_3 -action. Voluntary arrest may take place at any stage in the transitionary period between consciousness and unconsciousness. It may be and is, but very infrequently, the last act of consciousness. The possibility of its occurrence is an argument against the rapid method of inducing unconsciousness; because, when it does occur, it is essential that the several components of the respiratory machine shall be in a normal condition—*i.e.*, normal so far as respects the action of CHCl_3 . The Rapid Method tends to produce, 1, respiratory overdose; and, 2, pulmonic congestion. If, therefore, voluntary arrest occurs in these abnormal circumstances, the subsequent state of the respiratory machine is not simple but complex, and it becomes a matter of necessity, in order to arrive at its true causation, to analyse it into its components. And when voluntary arrest chances to be the last act of consciousness, it is to be remembered that the

result on the respiratory centre continues for a short interval after the onset of unconsciousness.

Functional or reflex arrest of the action of the respiratory centre may occur and does so, when the circumstances are favourable, in the course of unconsciousness. The action of the respiratory machine is suddenly arrested at the end of a full inspiration, which is the invariable antecedent of the act of vomiting, or at some stage during its progress. The former happens in normal anæsthesia, in which the act of vomiting is uninterrupted. The latter happens in abnormal anæsthesia—*i.e.*, anæsthesia complicated either with a temporary respiratory overdose or mechanical obstruction, or both, and in narcosis. In one, full respiration is prevented by obstruction in the air-way—in the other, by (physiological) pulmonic congestion. In both, the removal of the disturbing factor is followed by completion of full inspiration and the act of vomiting. These instances of respiratory arrest are thus perceived to be complex in their nature. They are invariably accompanied by a fall of blood-pressure, which is manifested in anæsthesia in the appearance of pallor, and in narcosis in that of lividity. The act of vomiting is immediately followed by the rapid return of blood-pressure to the

normal,—a fact which proves that it is of reflex origin.

Besides sudden arrest, there are instances of rapid arrest of the respiratory movements. And as these are preceded by increased respiratory vigour, it might be concluded that prolonged stimulation of the respiratory centre is followed by its exhaustion. But against this conclusion the following arguments may be brought. Though there is evidence of the stimulation of the respiratory centre, there is no strong proof that CHCl_3 is the direct cause of it. Secondly, it is accepted that the energy of the respiratory centre is relatively inexhaustible. Thirdly, the phenomena, antecedent to arrest, are assumed to be characteristic of its condition of exhaustion. But are these phenomena actually associated with this condition? This is the matter in dispute. The assumption that the respiratory centre is exhausted explains the arrest of respiratory movements, but it leads to the weakest form of reasoning—viz., the circular argument. Besides, it prejudices the causation of respiratory arrest by favouring one agent. Where the factors involved in the production of a given phenomenon are many, as, 1, the respiratory centre; and, 2, the several components of the respiratory machine, in the

causation of respiratory arrest, it is conceivable that the cause may proceed from any one of them. Thus exhaustion of the motor-power of the respiratory machine may be a cause of respiratory arrest. Before, therefore, we conclude that exhaustion of the respiratory centre is the cause, it will be necessary to exclude the presence of exhausted respiratory muscles, or, if the latter are exhausted, to prove that their abnormal condition is not the chief cause of respiratory arrest. And so with every other conceivable cause or combination of causes.

Again, there is no uniformity among instances of respiratory arrest considered generally. They show differences in their mode of onset, and in the phenomena accompanying them. But when classified into groups uniformity appears among the members of each group. Which group, then, is connected with the exhausted condition of the respiratory centre? There is obviously a difficulty here, for it is not known what the progress of the phenomena is in this abnormal condition. But the difficulty is removed by taking an instance from each group, and observing the attitude of the respiratory centre during and after the application of artificial respiration. Before the resumption of spontaneous respiration there is an attempt, but

an ineffectual one, at respiration. But the state of the respiratory machine is not yet favourable to the manifestation of the activity of the respiratory centre, for these reasons. Pulmonic congestion is not completely removed, and the supply of oxygenated blood to the respiratory muscles is not as yet sufficient to enable them to resume their function. When, however, spontaneous respiration reappears, the action of the respiratory machine almost immediately reaches the normal. From this fact the inference is certain that the activity of the respiratory centre is normal. If, therefore, the respiratory centre has been exhausted, it recovers its normal function with a rapidity that is contrary to the experience derived from the recovery of other exhausted nerve-centres. For that experience teaches us that recovery from the condition of exhaustion is essentially gradual. In these circumstances the rational inference is that the respiratory centre is prevented from manifesting its activity through the abnormal state of the respiratory machine.

CHCl_3 , by its negative action, is related to the respiratory centre. A proportion of air is displaced, and is followed by a corresponding diminution of the amount of oxygen absorbed into the blood. The variations thus respect-

ively induced in the volumes of OXY and CO_2 are invariably associated with increased activity of the respiratory centre, which is reflected in increased frequency of the action of the respiratory machine. But when the CHCl_3 -air atmosphere is discontinued, its negative action ceases as soon as CHCl_3 disappears in the airway. Let us suppose that an interval of 30" is needed for this purpose. There being then no impediment in the process of the absorption of the normal amount of oxygen, the blood will soon become normally oxygenated, and, consequently, the respiratory centre, released from temporary stimulation, will resume its normal activity. A short interval will be needed after the cessation of the negative action of CHCl_3 , and before its result entirely disappears—*i.e.*, before the blood becomes normally oxygenated. An interval of 15" is allowed for this procedure. Thus, at the end of 45" after the withdrawal of CHCl_3 , the frequency of respiration should be normal if the respiratory centre is only negatively affected by its action. But the fact is that the respiratory frequency is appreciably diminished on the cessation of CHCl_3 -action, and the progress of its diminution continues without interruption until it reaches the normal at the end of 5'. Its return to the normal is

thus relatively gradual, as compared with the rapid return in the case of the simple negative action of CHCl_3 considered in the abstract. If, therefore, the respiratory centre is affected only by alterations in the proportions of the O_2 and CO_2 constituents of the blood during CHCl_3 -anæsthesia, the fact that, after the cessation of CHCl_3 -action, the blood requires a longer interval than can be justly attributed to negative action in which to become normal, proves that there is a factor present which delays the process of reoxygenation after the disappearance of the negative result.

The causation of the increased respiratory frequency accompanying CHCl_3 -action is thus shown to be not simple but complex. 1. There is the negative action of CHCl_3 , resulting in the reduction of the volume of oxygen in the blood; and, 2, there is its physiological action, for there is no other cause present than CHCl_3 , and of its three spheres of action, the physical one is excluded by the absence of impairment of aeration. Both these actions lead to deoxygenation of the blood, but in different ways: the negative, by diminishing the amount of oxygen absorbed; the physiological, by reducing in some as yet undefined way the volume of oxygen in the blood. The negative action is

not so potent as the physiological, because its result on the blood disappears more rapidly. Of the negative and positive CHCl_3 -factors which are associated in the production of increased respiratory frequency, the latter now appears as the chief cause of it, and the difficulty which was presented by the former is overcome. The first phenomena to appear in the course of CHCl_3 -action is increased respiratory frequency. There is a cause to explain it in the displacement of air by the vapour of CHCl_3 . Consequently doubt exists concerning the fundamental phenomenon of its physiological action. But as soon as it is isolated, by analysing complex results into their simple components, and demonstrating what part is due to the physiological and what to the negative action of CHCl_3 , the course of the investigation will become clear. The fundamental phenomenon of the physiological action of CHCl_3 is the same as that of its negative action—viz., increased respiratory frequency. Increased respiratory frequency is the necessary consequence of stimulation of the respiratory centre. The physiological action of CHCl_3 is thus causally connected with stimulation of this centre. A causal connection is either direct or indirect. That is to say, CHCl_3

is absorbed into the blood, and is either carried to the respiratory centre, which it directly affects, or the direct result of its action on the blood—deoxygenation—becomes an intermediate cause of respiratory stimulation. There is no very strong proof in favour of the direct action of CHCl_3 on the respiratory or any other nerve-centre. But a very strong objection can be produced against it. The frequency of respiration, after a period of comparative stability, tends to increase in the course of anæsthesia. But to maintain the state of anæsthesia, it is necessary to diminish progressively the degree of CHCl_3 -action. A diminishing degree of CHCl_3 -action is associated with constancy in respiratory frequency at first, and afterwards with inconstancy. If CHCl_3 affects directly the condition of the respiratory centre, incongruity appears in a less degree of CHCl_3 -action, causing an increase in the degree of stimulation of the respiratory centre, unless it be shown that that centre has undergone a change of condition. Again, the same degree of CHCl_3 -action being maintained, the frequency of respiration is after a period increased, and tends to become more so as the duration of unconsciousness is prolonged. Now the same degree of intensity of a cause is synonymous with the

same degree of its effect. If, then, the condition of the respiratory centre remains undisturbed, except by CHCl_3 , the same degree of its action will necessarily be followed by a constant degree of increased respiratory frequency throughout the period of unconsciousness. And if at any stage, whether early or late, the degree of action is diminished and there is nothing to prevent its necessary consequence from appearing—viz., corresponding diminution in the degree of effect—the frequency of respiration will be reduced to a lower degree, and remain constant in that degree. But though small variations, either of increase or decrease of CHCl_3 -action are immediately followed by their respective variations of the frequency of respiration, which might point to an assumed direct but delicate relationship between CHCl_3 and the respiratory centre, yet the resulting respiratory variations do not continue constant, but tend universally to increase their degree.

The result of CHCl_3 -action on the respiratory centre is determined by the effect of CHCl_3 on it, and the actual condition of the centre. When the degree of CHCl_3 -action is constant, but respiratory frequency tends to increase, it becomes necessary to refer the source of

the latter to some change in the condition of the centre, on the supposition that CHCl_3 directly affects it. The change is manifested by a tendency to increased action independently of the influence of CHCl_3 . The hypothesis that CHCl_3 directly stimulates the respiratory centre fails, therefore, in its function, which is the explanation of all the facts connected with respiratory variations. And it follows as a consequence thereof that the causation of these changes is to be found in the indirect action of CHCl_3 , which produces an intermediate cause which explains not only the initial increased frequency of respiration which results on the action of CHCl_3 , but also its tendency to increase still further in the course of that action, when it is maintained at a constant degree.

Supposing that CHCl_3 causes deoxygenation of the blood, for it is not yet experimentally proved to do so, the following facts become significant: I. Oxygen is abstracted from the blood without interfering with the efficient action of the respiratory machine. II. The blood is capable of undergoing certain degrees of reduction in the volume of its oxygen without any apparent change of its colour.

§ 88. *Relation of CHCl_3 to the respiratory*

machine.—The frequency of the respiratory movements is directly controlled by the respiratory centre. But their character is determined by local abnormalities in one or other components of the respiratory machine. Abnormal movements may be simple or complex in their causation.

The air-way may be the seat of mechanical obstruction. Its source is generally in backward displacement of the base of the tongue. Particular causes of it are floating polypus in the pharynx, and foreign bodies, including matter, in the bronchi.

Some degree of mechanical obstruction from displacement of the base of the tongue is an invariable accompaniment of CHCl_3 -action, and is remotely related to it. Thus, CHCl_3 -action produces indirectly muscle-relaxation, and consequently upon its inefficient support the tongue gravitates and, in the progress of its displacement, encroaches upon the glottis. The degree of displacement is therefore determined by the actual condition of the muscles. In normal conditions it is the least possible at the commencement of anæsthesia. But as in its course the condition of the muscles undergoes a change, which is inferred from the progressive diminution of their tone, a tendency

is in existence to increasing the degree of obstruction. This tendency will manifest itself when circumstances are favourable to it. One of these is the prolonged duration of anæsthesia. Thus, at the end of 1°.5, signs of obstructed breathing appear. And they disappear on the removal of its cause—*i.e.*, on the replacement of the base of the tongue in its normal position.

The tongue may be abnormally large; the condition of the muscles may be initially abnormal. These are the circumstances that determine the early occurrence of mechanical obstruction in the initial normal condition of the air-way. But the latter may be obstructed by enlargement of the tonsils, but not so as to be associated with impairment of aeration. The occurrence of muscle-relaxation may, in this initial abnormal condition of the air-way, be quickly followed by complete mechanical obstruction, respiratory movements continuing, if it takes place at the end of expiration, but ceasing when it coincides with the completion of the act of inspiration.

However induced, and whenever it occurs, incomplete mechanical obstruction intensifies the results of CHCl_3 -action. And as its degree may increase so gradually as to produce no sharply-defined change in the state of anæs-

thesia—*i.e.*, the increasing degree of each of the phenomena proceeds so slowly as to be practically imperceptible—it becomes a source of perplexity. For mechanical obstruction leads to pulmonic congestion and deoxygenation of the blood. In the new condition of the blood, the proportion of CHCl_3 in the CHCl_3 -air atmosphere becomes, if initially anæsthetic, relatively narcotic; if initially narcotic, but not of such a degree as to be presently dangerous in itself, its degree becomes relatively increased, and may, in the altered circumstances, be dangerous. It follows, therefore, that the normal patency of the air-way is the chief safeguard in the administration of CHCl_3 . And that, in instances of its initial obstruction, the proportion of CHCl_3 is to be determined by the degree of deoxygenation which is present.

The air-way may also be the seat of physical obstruction—*i.e.*, there may be an excess of CHCl_3 -vapour in it. This is termed a respiratory overdose, in contradistinction to the excess of CHCl_3 in the blood, which is called a blood-overdose. A respiratory overdose may be absolute or relative. When there is too large a proportion of CHCl_3 in the CHCl_3 -air atmosphere—one of the defects of the Rapid Method—its physical action is reflected in the

prevention of normal respiratory movements. The weight of the mixed atmosphere to be expelled is too great for the power of the expiratory muscles. And thus when the proportion of CHCl_3 reaches its maximum in the air-way, its opposition to respiratory movements is at its greatest. The excess of CHCl_3 -vapour is removed, not by absorption into the blood, as might be supposed, but by diffusion into the atmosphere. And as the proportion of CHCl_3 becomes thus diminished, respiratory movements increase their range, and, because the removal of the respiratory overdose is rapidly effected, rapidly assume the degree of frequency which corresponds to the condition of the blood.

The Graduated Method avoids the production of an absolute respiratory overdose. But inasmuch as variations may occur in the action of the respiratory machine, proceeding from causes acting simultaneously with, but independently of, CHCl_3 , if the proportion of CHCl_3 be not adapted to the requirements of the altered component of the machine, a relative respiratory overdose will necessarily ensue. Thus stomachic inhibition of the respiratory centre and a relative respiratory overdose may concur, and their combined action lead to rapid

arrest of the respiratory movements. Again, a relative respiratory overdose may be present when functional arrest of the action of the respiratory centre occurs. As functional arrest is confined to one stage of the act of respiration—viz., the termination of a full inspiration—and as the presence of a relative respiratory overdose prevents its completion, respiratory movements will be suddenly arrested at an early stage in the act of inspiration, and will continue so until the respiratory overdose is removed. It is possible that this may be effected by diffusion, the air-way being rendered normally patent, if mechanical obstruction be present. The interrupted act of inspiration will then be completed, and immediately afterwards followed by the expulsion of the contents of the stomach.

The air-way may be obstructed not only simply mechanically or simply physically, but also by the combined actions of mechanical obstruction and a relative respiratory overdose. And the variety of combinations formed by different degrees of these two causes provides a datum for the explanation of the various degrees of rapidity with which respiratory arrest occurs.

In the case of abnormal lungs, a causal

factor is present and tends to impede the normal aeration of the blood. Consequently they are more than normally sensitive to variations of the proportion of oxygen in the CHCl_3 -air atmosphere. If the causal condition be of sufficient degree, it is conceivable that a small proportion of CHCl_3 will be followed by a large degree of pulmonic congestion, and that if the maximum be rapidly reached the tendency to respiratory arrest will be rapidly manifested. The causation of these forms of respiratory arrest is thus not connected with the positive but with the negative action of CHCl_3 , and resides in the rapid reduction of the means whereby the alveolar circulation is carried on—viz., of oxygen.

But a degree of induced pulmonic congestion may exist which is not in itself incompatible with a safe degree of respiratory inefficiency. It is associated with abnormally increased activity of the respiratory machine, formerly regarded as the normal accompaniment of CHCl_3 -action. More work, therefore, is done by the muscles of respiration than is absolutely necessary; and, as the inevitable consequence of overwork, a tendency to exhaustion appears in them, and is manifested by the coming into action of the extraordinary muscles of respira-

tion. While, however, the obstacle opposing their action increases, their blood-supply diminishes both in amount and quality—*i.e.*, the degree of deoxygenation of the blood increases. What actually determines respiratory failure in these instances is the reduction, below a given degree, of the oxygen-supply to the muscles. For when the amount of oxygen is increased, as by artificial respiration, their power will be gradually restored, and subsequently manifested by the performance of their functions.

The motor-power is capable of being adapted to slight variations in the constitution of an abnormal atmosphere without thereby losing its efficiency. But when the work to be done—*viz.*, the expulsion of a heavy atmosphere—is not proportioned to the actual power of the respiratory muscles, their result will become abnormal. And the abnormality will be manifested by the expansion of the chest.

The act of inspiration is associated with the tendency to the formation of a vacuum in the middle and lower air-way. Opposition to it exists in the pressure of the atmosphere which acts equally on the surface of the chest-walls. The act of expiration consists in the expulsion of the contents of the air-way through a narrow channel, at the external aperture of which it is

met by the resistance of the atmosphere. Its power is therefore concentrated upon a circumscribed area. If the weight of the mixed atmosphere in the air-way exceeds a certain degree, the expiratory act will be followed by the expulsion of less than the normal volume of contents. The residual contents will thus prevent the intake of the normal volume of the mixed atmosphere. The constitution of the mixed atmosphere in the air-way, so far as the proportions of the vapour of CHCl_3 and air are concerned, becomes different from that of the external CHCl_3 -air atmosphere. The difference arises in the tendency of the relatively heavy CHCl_3 -vapour to gravitate. Consequently the proportion of expired contents tends to become diminished. If, now, the relation between the intake and the output of the mixed atmosphere, which is respired, continued normal—*i.e.*, they are equal to each other—the condition of the chest, in respect of its size, would remain the same. But the fact is that it becomes expanded, and the degree of expansion tends to become increased under the operation of some causal condition. The conclusion, therefore, based upon the purely physical causation of the expansion of the chest—and there appears to be no other—is that, under the abnormal circumstances, the intake is larger

than the output. The following examples serve to demonstrate the validity of the conclusion. They are characterised by an accidental increase in the degree of resistance opposed to the act of expiration. I. Anæsthesia was induced in a young girl *ætat.* 14. About 5' after the commencement of the surgical operation (on the foot) the chest was observed to be expanded, and to continue to expand while the CHCl_3 -air atmosphere, the proportion of CHCl_3 in which had been reduced from 3 to 2 drops, was being administered. The degree of expansion subsequently becoming so great that respiratory movements were restricted to the abdomen, the position of the base of the tongue was investigated and found to be displaced backwards. On the restoration of the normal patency of the air-way the chest immediately collapsed. II. Laryngotomy had been performed in a fairly healthy male aged 56. 30' after the induction of anæsthesia, the proportion of CHCl_3 having been normally reduced to 3 drops, the tube became displaced as the consequence of a change of the patient's position, which was necessitated by the operation. Some difficulty was encountered in its replacement, and during the endeavour the chest was observed to be gradually expanding.

When at last the laryngotomy tube was replaced in its proper position, the chest immediately collapsed. Thus, in the circumstances of a heavy atmosphere and a mechanically obstructed air-way, there is no difficulty, or at least no predominating difficulty, opposing the act of inspiration, whereas the act of expiration is opposed by a resistance which it cannot completely overcome.

The causation of respiratory phenomena may be simple or complex. The cause or causes may be in some abnormal condition of one or more of the components of the respiratory machine. The cause may also be in some abnormal condition of the respiratory centre. It is necessary to determine, therefore, not only the relation between CHCl_3 -action and a given phenomenon, but also to explain the causation of all the phenomena which occur during it, but are not causally connected with it. Thus to every phenomenon if simple, or if complex to each component of it, its own cause is to be assigned. CHCl_3 may be the sole cause of the arrest of respiratory movements. It may also act in combination with an independent cause in producing the same result. But in neither instance can it be proved that it affects directly the condition of the respiratory centre. When CHCl_3 -

action is causally associated with respiratory arrest, it operates either directly in the air-way as an absolute or relative respiratory overdose, or negatively in the production of (physiological) pulmonic congestion, which may be complicated by the action of a reflex cause, or if uncomplicated and continued, will tend to the exhaustion of the respiratory muscles.

§ 89. *Relationship between CHCl_3 and the spinal centres.*—The following are the data which enter into the solution of this part of the problem.

Muscle-phenomena are not invariably present in the normal induction of anæsthesia. When they occur they do not always appear at the same stage, nor do they present the same character. Their presence is invariably accompanied by either, 1, a defect in the method of administration, or, 2, the method of administration being normal, either with (a) voluntary action or (b) an abnormal condition, becoming in the circumstances a causal factor.

Voluntary movements are not necessarily associated with duskiess. The administration is therefore continued, if at the beginning of voluntary struggling no duskiess is present. For that expression of voluntary opposition is not a contra-indication for the withdrawal of the agent, the end-object of the action of which

is the suspension of the cause that is opposing it. On the other hand, if duskiness be present with muscle-phenomena on their first appearance, or if it intervenes in the course of their progress, it will be an indication for either the withdrawal of CHCl_3 or the necessary modification of the method of its administration, in order to meet the particular requirements of abnormal conditions. For duskiness—*i.e.*, deoxygenation of the blood—may be associated with a particular kind of muscle-phenomenon. And unless all the circumstances which are favourable to their production are excluded, their origin will remain unknown. One of those circumstances is a respiratory overdose. If, therefore, the administration be continued when a respiratory overdose is present, the degree of the cause will be increased, and consequently there will follow an increase, directly proportioned to it, of its result.

This defect in the normal method—*viz.*, the production of respiratory overdose—may be present at any stage of the period of induction. When it occurs during the later stages—*i.e.*, when the function of the will is in abeyance—the muscle-phenomena dependent upon it are capable of being studied in their simple state. The fundamental character thus presented is

rigidity. And as the degree of duskiness tends to increase, so also does the degree of rigidity. If, now, a larger proportion of air is given or CHCl_3 is removed, duskiness tends to be diminished, and, with the alteration in the colour of the complexion, the muscles become less rigid, all rigidity disappearing on the return of the natural colour of the complexion. Thus duskiness and muscle-rigidity stand in the relation of antecedent and consequent, and the relation is an invariable one. Deoxygenation of the blood is known to be a cause of muscle-rigidity. But not in all circumstances. The particular circumstances in which it is so are, 1, the rapid production of, 2, a certain degree of, deoxygenation. The negative and physical actions of CHCl_3 are capable of causing, in favourable circumstances, such a degree rapidly. And it is precisely in these circumstances that muscle-rigidity appears. The causation of one kind of muscle-phenomena is thus connected not with the physiological, but with the combined negative and physical actions of CHCl_3 .

A causal condition may exist, and either not be isolated, or else its degree not accurately determined. The details of the normal method being framed for normal conditions, if one of

these be abnormal, but no adaptation is made in the particular detail affecting it, the result upon it will necessarily be abnormal. The initial abnormal condition—*e.g.*, atrophic emphysema—will be converted into a causal factor. The normal method thus becomes, relatively to this abnormal condition, rapid. The reduction of the proportion of air being too rapidly effected, the lungs become congested. When abnormal lungs are congested, they require, in the presence of air, a relatively longer time than initial normal ones for the purpose of unloading. But a CHCl_3 -air atmosphere is present in the air-way, impeding the function of aeration. The interval is therefore prolonged by the length of the period which is needed for the diffusion of CHCl_3 vapour into the external atmosphere; and during it the blood becomes rapidly deoxygenated. In one instance the normal method was associated with the early appearance of rigidity before the maximum proportion of CHCl_3 was reached; the abnormal condition of the lungs not being known, CHCl_3 was removed. But its removal was followed not by the progressive diminution of rigidity, as would happen in normal conditions, but by its progressive increase, culminating in opisthotonos. The air-way

being maintained normally patent, all traces of muscle-rigidity eventually disappeared. The necessary modification of the method being made in the second administration, anæsthesia was induced and maintained without the appearance of muscle-phenomena.

Anæsthesia may be induced without the appearance of muscle-phenomena. There is, therefore, negative proof that the condition of the spinal centres, assuming that it is abnormal, is not one of stimulation. Anæsthesia may be converted into narcosis, and yet without the occurrence of any objective muscle-phenomena, the only change taking place in the muscles being diminution of their tone. From this, however, it cannot be concluded that the spinal centres are paralysed, for there is no direct connection between the paralysis of motor-centres simply and the vitality of the muscles, the functions of which they control. The connection is indirect. Muscles tend to atrophy because they are not used. They are not used because the centres, being destroyed, cannot actuate them. But the tendency to atrophy may be counteracted by artificial means.

The Rapid Method is responsible for the notion of the (misnamed) CHCl_3 -convulsion. Its object is to induce unconsciousness as

quickly as possible, so as to remove that cause in particular which exercises an influence on the progress of CHCl_3 -action—viz., volition. In the endeavour to overcome one difficulty, however, another and more formidable one was created. For the rapid concentration of CHCl_3 -vapour is of necessity associated with the undue influence of its physical action in the air-way. But this inherent defect of the method is not only followed by its own direct result—viz., the formation of a more or less complete barrier between the internal alveoli and the external air—but it also leads to (secondary) voluntary inhibition of respiration, which is greater or less according to the degree of the effort that is opposed to a suffocating atmosphere. Thus, the rapid absorption of CHCl_3 into the blood is prevented; for that implies, at least, the normal state of the alveolar circulation. But the combined results of respiratory overdose and voluntary inhibition tend to its obstruction. The blood, consequently, is affected by the actions of two different causes. It is deoxygenated, and more or less rapidly deoxygenated, by the absence of a sufficient supply of air to the alveoli. And it is directly affected by the amount of CHCl_3 that is absorbed into it. The muscular phenomena ap-

pearing in the progress of the Rapid Induction of unconsciousness—for not a simple CHCl_3 , but a complex result is produced—are therefore associated with the presence of two possible causes, either of which or both combined may produce them.

If CHCl_3 , by its direct action on the spinal centres, is assumed to be the ultimate cause of convulsive movements, followed, first, by tonic spasm and afterwards by paralysis of the muscles, it follows that these phenomena should appear in the same order, in all circumstances in which CHCl_3 is acting, provided that no one of them interferes with their production. But they do not appear in anæsthesia, in which all the circumstances are favourable to the simple action of CHCl_3 on the spinal centres, and there are none to complicate it. If, against this, it is argued that the degree of CHCl_3 -action is not sufficient, and that in CHCl_3 -narcosis there is evidence of the paralysed condition of the centres in the assumed paralysis of the muscles, the answer is that the muscles are paralysed without the antecedent manifestation of convulsive movements and tonic spasm, and therefore that the antecedent condition to their exhaustion—viz., stimulation—is absent. If, therefore, the

actual condition of the spinal centres is one of paralysis, and CHCl_3 is the cause of it, its mode of operation is not invariably the same, for in some instances stimulation precedes paralysis, in others paralysis occurs without antecedent stimulation. This argument irresistibly refutes the conclusion that CHCl_3 -action is directly related to the spinal centres. And it is accompanied by another not less convincing. In spastic rigidity of the lower extremities the condition of the spinal centres is abnormal, and such as to be more than normally sensitive to the influence of a direct stimulus. If, then, CHCl_3 be administered, there should be an increase of the degree of the muscle-abnormality, followed by paralysis, if it exerts a stimulant effect upon the spinal centres. But the fact is that while the muscles of the upper extremities become relaxed, those of the lower remain unaffected.

One group of muscle-phenomena is invariably preceded by deoxygenation of the blood. Changes in the degree of one of these factors are associated with, and directly proportioned to, changes in the degree of the other. A causal relation thus exists between them, and the occurrence of rigidity in the progress of the induction of unconsciousness will consequently be

an indication of fault in the method. For the Normal Method does not conduce to struggling, which complicates the simple action of de-oxygenated blood on the muscles. The fault consists in the abnormal increase of the proportion of CHCl_3 at a particular stage of the induction, and its consequence is the production of a respiratory overdose. The removal of its proximate cause, effected by diffusion into the external air, will be followed by the return of the normal colour of the blood, and the disappearance of muscle-rigidity. CHCl_3 -action, therefore, has no positive relation to muscle-rigidity, which is not necessarily, but only in certain circumstances, a concomitant of its physical action. A fundamental error is committed in not including all the factors that invariably accompany any given phenomenon, the causation of which is the object of investigation. CHCl_3 has three spheres of action—negative, through its displacement of air, physical in the air-way, and physiological. It is essential, therefore, to exclude both its negative and physiological actions before we can conclude that a given phenomenon is derived from its physiological action, or in the case of a complex CHCl_3 -result, to prove that either of the former is unequal to produce the whole of it.

§ 90. *The relation of CHCl_3 to reflex-action.*—Three kinds of reflex-action may occur during the administration of CHCl_3 —ideo-motor, sensori-motor, and vaso-motor. It will be necessary to examine these severally in all their details.

I. Ideo-motor. The emotional state may be present at the commencement of induction, and become increased in intensity during its early stages. Its origin is in primary stimulation of the cardio-inhibitory centre, and it is accompanied by indirect fall of blood-pressure and secondary acceleration of respiratory frequency as its intimately related phenomena. The remotely related phenomena are dilatation of the pupil, muscle-relaxation, and perspiration.

The tendency of CHCl_3 -action is to suspend, along with the other functions of mind, that of the emotional centre, in which arises the stimulus which is reflected to the cardio-inhibitory centre. Consequently the degree of the emotional state tends to become diminished, and on the suspension of its ultimate cause it will disappear. But its complete disappearance does not coincide with the onset of anæsthesia. A short interval will elapse before the pulse resumes its natural frequency and the pupil becomes normally contracted. The fact that the lower centre remains in a condition of dis-

turbance after the higher one which actuates it ceases to operate, is to be considered with reference to the pulse-record at the onset of anæsthesia, and the necessary interval allowed to elapse in order to arrive at a pure CHCl_3 -result.

The pulse, therefore, will in this kind of initial cardiac abnormality undergo a diminution of frequency—*i.e.*, it becomes stronger. And the cause of the change might be ascribed, but erroneously, to the influence of CHCl_3 .

The degree of the emotional state varies in intensity. And its degree may be such as to be associated with an impairment of the action of the respiratory machine that is antagonistic to the physical action of CHCl_3 . Seeing that the respiratory machine is the medium by which CHCl_3 is introduced into the blood, it will be absolutely imperative, in these instances, to defer the administration until its action becomes favourable. In fact, intense emotion in itself is, in some circumstances, dangerous to life. On two occasions death occurred while preparation was being made for the administration of CHCl_3 .

II. Sensori-motor. In anæsthesia the same degree of stimulation of the sensory nerve is associated at different times with different degrees

of muscle-contraction. In the early stages of it muscle-contraction is apparently normal. But in the later stages the degree of contraction becomes diminished, the tendency to diminution increasing with increase in the duration of anæsthesia. The same tendency appears in narcosis. But as compared with anæsthesia, there is this initial and characteristic difference—viz., the same degree of nerve-stimulation in narcosis, in its early stages, is accompanied by a less degree of muscle-contraction than that which obtains in the corresponding stage in anæsthesia. In different degrees of narcosis, the degree of muscle-contraction differs when the experiments are conducted under the like circumstances—viz., the degree of nerve-stimulation is the same, and comparison is limited to the results obtained in corresponding stages in the course of different degrees of narcosis. Thus a conclusion with respect to muscle-contraction will be true for one set of circumstances only.

In the higher degrees of narcosis there is no muscle-response to nerve-stimulation, though it be intense. But in moderate degrees an increase in the intensity of the stimulus is followed by a proportionate increase of muscle-contraction. It might be concluded, therefore, supposing that no series of consecutive observa-

tions were made, that the spinal centres are the seat of lesion in the sensori-motor circuit. For the assumed degree of their depression is proportionate to the degree of CHCl_3 -action. And this is one of the characters of a causal connection.

The factors concerned in sensori-motor reflex-action are—1, the degree of the stimulus conveyed by the sensory nerve; 2, its reflection by the centre into the motor nerve; and, 3, muscle-contraction. Normal reflex-action presupposes the normal condition of each of these factors. If, therefore, the application of a stimulus is followed by no result, or by a degree of muscle-contraction less than that which normally accompanies it, the lesion will be either in the sensory or motor nerve, or in the centre, or in the muscle. For it is conceivable that the condition of the muscle may be unfavourable to the effect of a stimulus reflexly conveyed to it.

From the fact that a stimulus applied to a motor nerve is followed in narcosis by muscle-contraction, the inference may be drawn that the lesion is not in it, and by implication not in the sensory nerve.

An abnormal condition of the centre leads to delay in the transmission of the stimulus, and to a modification of its intensity. These results

appear in narcosis. The muscles are not so sensitive to reflex-stimulation—*i.e.*, the interval between the application of the stimulus and contraction is prolonged beyond the normal—and the progress of their contraction, instead of being rapid, as it is normally, is sluggish. Now the actual condition of the centre can only be determined by an inferential argument. The centre is, on supposition, in a condition of depression or paralysis, the cause of which is the direct action of CHCl_3 on it. But in instances of the higher degrees of narcosis, reflex-action is restored to the normal in a comparatively short time—the comparison being made with the prolonged period that elapses before the centre recovers its function after being paralysed by an agent which is known to have a direct influence upon it. The circumstances, then, affecting recovery in these examples are not alike, as they would be if the abnormal condition of the centre were the same in both. The inference, therefore, in the case of CHCl_3 , is that the spinal centres are not the seat of the lesion. But in all experiments relating to sensori-motor reflex-action in the state of narcosis, the muscles are in an initial condition of abnormality. Now the conduct of the muscles is taken as evidence of an assumed condition

of the spinal centres. But the influence of the abnormal muscle is not excluded. That influence, however, is of such a nature as to affect its powers of contracting. For it proceeds from impairment of nutrition. And impairment of nutrition is synonymous with impairment of function. The different degrees of CHCl_3 -action which are associated with different degrees of an assumed depressed condition of the spinal centres are also associated with different degrees of impairment of muscle-nutrition, and are directly proportioned to each other. In the case of the spinal centres this causal connection involves the assumption of the cause—viz., paralysis of the centres. Whereas in the case of the muscles, a cause which affects muscle-tone is demonstrated to be in existence. If, then, it can be proved that this cause—viz., deoxygenation of the blood—is sufficient to explain the results that are implicated, the lesion existing in the sensori-motor circuit, in narcosis, will be located in the muscles.

III. Vaso-motor. The occurrence of falls of blood-pressure is only occasional during CHCl_3 -action. That it originates, in the majority of instances, in stimulation of the vaso-motor centre, is proved by the course of the phenomena, which appear subsequently to it, agreeing in

all respects with the return of the blood from the portal to the main circulation in vaso-motor fault. Thus, in an uncomplicated example, primary fall of blood-pressure is followed by a rapid decline of the action of the respiratory machine to its minimum and complete dilatation of the pupil. The air-way being normally patent, the return of the action of the respiratory machine to the normal is effected slowly, and is characterised at its commencement by the rapid contraction of the pupil, and during its course by the reappearance of the pulse. Stimulation of the vaso-motor centre, when it occurs during CHCl_3 -action, is invariably associated with disturbance in some part of the sympathetic system produced in the progress of the surgical operation. Its reflex origin is thus defined.

The return of the blood from the portal to the main circulation is delayed or interrupted respectively by the impairment or arrest of the function of aeration, which may be effected in different ways. These are—1, the backward displacement of the base of the tongue; 2, the presence of an excess of CHCl_3 -vapour in the air-way, temporary respiratory overdose; and 3, (physiological) pulmonic congestion. One of the concomitants of reflex stimulation of the

vaso-motor centre is collapse of the muscles. And one of its results is mechanical obstruction in the air-way. In vaso-motor complication, therefore, the chief concern is the normal patency of the air-way, which of necessity has to be effected artificially. If this be not done, or done inefficiently, the blood from the right side of the heart, instead of taking its normal course through the alveolar circulation, will be deflected into the main veins, and consequently lead to distension of the superficial ones.

But it may happen that in vaso-motor complication occurring during normal anæsthesia, the immediate removal of mechanical obstruction is not immediately followed by the recovery of abdominal movements. But they do so after an appreciable interval, or the artificial expulsion of the respiratory contents. Some obstacle, therefore, opposes the commencement of the natural process of recovery. And as there is but one means by which this can be produced—viz., obstructed alveolar circulation—which, again, can only be caused generally by the absence of a sufficient supply of air to the alveoli, it follows that the obstacle removed operates by preventing or retarding this supply. But there are, at the time, only two factors present in the air-way, and by consequence

there is not sufficient air. The presence of an excess of CHCl_3 -vapour in the air-way thus explains the circumstance of delay in the process of recovery.

Pulmonic congestion is not one of the components of the state of anæsthesia, but it is an important component of the state of narcosis. And its degree varies directly with the degree of narcosis. Reflex-stimulation of the vasomotor centre may occur during narcosis. In that contingency, primary fall of blood-pressure concurs with pulmonic congestion. But pulmonic congestion opposes the return of the blood to the main circulation.

The degree of pulmonic congestion may not be sufficient to affect the action of the respiratory machine in more than a moderate, and therefore not immediately dangerous, degree. But if it should happen that blood-pressure falls during this abnormal condition, respiratory action will be arrested simultaneously with or rapidly after it, and it will show no sign of spontaneous recovery.

The respiratory muscles are suddenly deprived of their blood-supply. They are thus in a most unfavourable position in regard to the performance of their function. But suppose that they do begin to recover, and their progress will be

necessarily slow, they are confronted by a relatively insuperable obstacle in the form of pulmonic congestion. The circumstances, then, determining their failure are, 1, initial deprivation of their blood-supply; and, 2, the presence of pulmonic congestion tending to continue it.

Pulmonic congestion is removed by artificial respiration. The interval necessary for its removal varies according to its degree: the less the degree, the shorter the interval, and the greater the degree, the longer the interval before the resumption of spontaneous respiration. There is a difference in the length of the interval which elapses before the recovery of spontaneous respiration with artificial means in instances of respiratory arrest occurring during CHCl_3 -narcosis. The difference is explained by the difference in the degree of narcosis. For the degree of pulmonic congestion determines the length of the interval, and is directly proportioned to the degree of narcosis.

Thus, one of the objects of inductive investigation is attained by isolating the independent causes which may accompany CHCl_3 -action. For that study is concerned not only with the action of the agent which is to be elucidated, but also with the explanation of all the phenomena which are associated with it,—their

causation, and all the circumstances affecting them. Thus CHCl_3 may exercise no influence on vaso-motor disturbance occurring during its action. Such is the case when its action is limited to the degree of anæsthesia. On the other hand, it may complicate one of the results of such disturbance, as, for example, the reduced action of the heart. And it may do so in one of two ways: either by its physical action in the air-way—temporary respiratory overdose, or by causing negatively pulmonic congestion—the narcotic degree of its action. But it will be perceived that in neither of these ways is its physiological action primarily implicated.

§ 91. *The relationship between CHCl_3 -action and the heart.*—Far too much importance has been given to this part of the problem. CHCl_3 has not been proved to act directly on the heart by demonstrative reasons. But the assumption that it does so has this adverse consequence; it tends to obscure the proper lines which the investigation of its physiological action should take.

The chief sources which gave rise to that ill-founded hypothesis are—1, the want of accurate and complete analysis, not only of all the phenomena, but also of all the circum-

stances under which they occur, which attend the disappearance of the pulse; and 2, the singular conclusion that CHCl_3 is the only agent or cause present, and acting, on all occasions of fall of blood-pressure.

In primary cardiac syncope, the function of the heart ceases, and its cessation is permanent. The mode of onset of its failure is invariably sudden. In reflex stimulation of the vaso-motor centre, the action of the heart is reduced to a minimum, and its subsequent attitude will be determined by its surroundings. If these be favourable, it will gradually but progressively return to the normal performance of its duties. But if an abnormal condition of the alveolar circulation be present at the onset of complication, or immediately follows it, the heart will be prevented from recovering its functional activity. There is a possibility, therefore, arising from the degree of intensity of the opposing cause, and from the incidence in point of time at which it begins to act during cardiac depression, of the heart manifesting no signs of recovery, or of failing after having manifested some signs of vigorous but ineffectual power. If, however, the cause opposing the natural recovery of the action of the heart be removed,—and it will be obvious that no delay should

take place in the application of the means which effect its removal,—the heart will gradually regain its function, and the fact that it reaches the natural condition of its activity within a very short space of time proves that its muscle has not been primarily affected.

Now, the phenomena which follow upon fall of blood-pressure, occurring in the course of CHCl_3 -action, are not exactly the same in every respect in all instances of it. If they were so, and were also accompanied by non-recovery of the heart, though artificial means of restoring respiration be efficiently applied immediately after the disappearance of the pulse, there would be some ground for inferring that CHCl_3 acts directly on the heart. But the inquiry is rendered more intricate by the following facts: 1, CHCl_3 possesses two different kinds of action—the anæsthetic and the narcotic; the difference consisting in the introduction of its negative action into the latter, in which there is also a higher degree of its physiological action than in the former; 2, The anæsthetic action of CHCl_3 is not causally connected with fall of blood-pressure; 3, the narcotic action of CHCl_3 varies in degree according to the quantity of the overdose, and the higher degrees of it are causally associated in certain

circumstances with secondary cardiac syncope. It will be imperative, therefore, to exclude the negative before that result can be ascribed to the physiological action of CHCl_3 .

Thus, the pulse may disappear at no definite stage in the course of anæsthesia, the antecedent condition of the circulation having been normal. It may also disappear in the course of narcosis, but on this occasion the antecedent condition of the circulation will have been abnormal. But the mode of its disappearance is different, being invariably sudden in the former and invariably rapid in the latter. Now, the mode of onset is the differentiating factor between different kinds of pulse-disappearance.

It will be necessary, therefore, to classify instances of pulse-disappearance into two main groups—1, those which occur rapidly, and 2, those which occur suddenly.

The members of the first group present uniformity in all fundamental respects—the phenomena antecedent to, accompanying, and following upon the rapid disappearance of the pulse being exactly alike. The following is a typical example of it: the tension of the pulse is increased, the blood is deoxygenated, and the pupil dilated antecedently to its disappearance; and as these phenomena undergo an increase

in the degree of their intensity, a direct proportion is seen to exist between their corresponding variations. The activity of the respiratory machine is increased, but its course is not regular, for at a stage before the onset of pulse-failure the intercostals manifest signs of declining action, while the extraordinary muscles of respiration come into operation, and venous distension appears and increases in intensity. The conditions accompanying the rapid disappearance of the pulse are—1, widely dilated and sluggish pupil; 2, an intense degree of discoloration of the blood; 3, partial disablement of the respiratory machine; and 4, venous distension. The phenomena appearing subsequent to the rapid failure of the pulse are—1, rapid arrest of the embarrassed action of the respiratory machine, and 2, an increase in the degree of venous distension.

A difference is found to exist on comparing the lengths of the period at the end of which pulse-disappearance takes place: it is short in some, longer in others. But it is not fundamental, inasmuch as it is determined by the actual degree of intensity of the agent: thus, a high degree of the narcotic action of CHCl_3 is associated with a comparatively short period, while a moderate degree of that action requires

a longer one to produce pulse-failure. Another difference consists in the circumstance that pulse-failure is not coincident with the commencement of narcotic action, but appears after a longer or shorter interval, when the same degree of narcotic action is continued. But it also is not fundamental for this reason: the degree of narcosis induced by the continuous action of the same degree of narcotic action does not remain the same, but it increases progressively in degree of intensity. When, therefore, pulse-failure occurs, the conditions are different from those which obtain at stages antecedent to it. The difference is one of degree only; but the influence of the changed conditions determines the degree of result when the action of the agent is maintained constant. The differences, therefore, which are observed and which might be adduced as evidence of the irregular action of CHCl_3 , will be perceived to be due to the different circumstances that may affect its action.

But in the second group—viz., that which is characterised by the sudden disappearance of the pulse during anæsthesia—there is no such uniformity amongst all the members of it, as there is in the first. It will be necessary, therefore, to divide it into sub-groups,

each of which will contain all those examples which possess identical characters. The result of such classification leads to the formation of the following sub-groups in which there are no antecedent abnormal phenomena: I. The sudden disappearance of the pulse is accompanied by immediate and wide dilatation of the pupil; the veins are empty; the action of the respiratory machine is not at first perceptibly affected. Subsequently, the action of the respiratory machine gradually declines; no change appears in the veins which remain empty; the pupil remains dilated, and there is no evidence of functional activity of the heart. II. The sudden disappearance of the pulse is accompanied by immediate and wide dilatation of the pupil; the condition of the veins is normal; the action of the respiratory machine is immediately affected, and subsequently it rapidly declines to a minimum. If the air-way is normally patent, the pupil is rapidly contracted to the normal, and the functional activity of the heart is manifested by the returning colour of the complexion.

The differentiating factor between these sub-groups is found in the attitude of the respiratory machine. In normal examples—viz., the occurrence of complication during anæsthesia—it

is unaffected, and, consequently, the action of the respiratory machine pursues the course that is determined for it by the influence of the complicatory agent alone. But the action of the respiratory machine may be abnormal when there is a sudden fall of blood-pressure; or when the fall is rapid, as in simple CHCl_3 -narcosis, a complicatory factor may intervene and affect the abnormal action of the respiratory machine. It will be obvious, therefore, that in these contingencies the result upon the pulse will be complex—*i.e.*, it will be affected by two complicatory agents.

In CHCl_3 -narcosis, in which the action of the respiratory machine is invariably abnormal, the intervening complicatory agent may take the form either of a temporary respiratory overdose, or of mechanical obstruction, the consequence of backward displacement of the base of the tongue. Both these factors tend to arrest the action of the respiratory machine; and the different circumstances that influence their operation—such as, 1, the degree of their intensity; 2, the length of time over which they act; and 3, the more or less rapid or gradual rate of increase of their intensity—serve to explain the differences which appear in the failure of the pulse from this complex causation.

In the case of sudden disappearance of the pulse during an abnormal condition of the respiratory machine, the abnormality may be, 1, mechanical obstruction in the air-way; 2, a respiratory overdose; or, 3, a moderate degree of pulmonic congestion, the consequence of the narcotic action of CHCl_3 . And it will be perceived that all these factors exercise an influence on the rapidity with which the pulse reappears through impairment of the function of aeration. Thus, the degree of intensity of a respiratory overdose, if moderate, will require a short interval, 2" or 3", in which to become dissipated, and will consequently postpone the reappearance of the pulse. On the other hand, pulmonic congestion requires a comparatively longer period for its reduction. The rate of oxygenation of the blood is consequently slower, and a longer interval elapses before the pulse reappears.

In simple instances of pulse-disappearance, therefore, its origin may be in the agency of CHCl_3 , but when it is so it is invariably associated with its narcotic action, and with the higher degrees of it; or it may not be causally connected with CHCl_3 at all, for the occurrence of fall of blood-pressure during CHCl_3 -anæsthesia is only occasional; but in order to

be causally associated with its action it should be invariable.

In complex instances of pulse-disappearance it will be essential to analyse each result into its proper components. Thus, the return of the pulse in a given instance is delayed. The cause of the delay is present and operating when the pulse fails. It is associated with one of the abnormal conditions that may accompany fall of blood-pressure. When the actual abnormal condition, which becomes a causal factor, is removed, the pulse will reappear, but with different rates of rapidity, which are the indications of different kinds of disturbing factors. And if artificial means are needed to restore the action of the respiratory machine, these will indicate the presence of the causal factor in a high degree of intensity. The causal factor thus being isolated, it will be essential to consider its relation to the action of CHCl_3 . It may be the consequence of its physical action. Thus, CHCl_3 will act directly in one sphere of its influence, and postpone the reappearance of the pulse. Or it may act negatively, and through the intermediation of pulmonic congestion oppose greater or less resistance, according to the greater or less degree of the abnormality, to the return of

the blood from the portal system. Or it may act physiologically, but indirectly, and, by producing an undue degree of muscle-relaxation, effect the backward displacement of the base of the tongue, the consequence of which will be an interference with the function of aeration, already in an abnormal condition.

But muscle collapse is a concomitant of fall of blood-pressure. The mechanical obstruction in the air-way, resulting from the displaced base of the tongue, may be complete or nearly so. Thus, in anæsthesia, complicated by vasomotor depression, the supply of oxygen to the alveoli will be restricted to the contents of the air-way below the obstruction. So long as oxygen is absorbed, the reduced action of the heart will manifest signs of increasing activity, and even the pulse may become perceptible at the wrist. But if the source of obstruction be not removed within a given interval, the absence of oxygen in the alveoli will be followed by the decline and arrest of the cardiac function. Thus, the pulse will again disappear after its reappearance. It will be perceived, therefore, that the determinant of the subsequent attitude of the heart is the nature of the respiratory contents. When these are normal—*i.e.*, there is no temporary respiratory overdose at the

onset of fall of blood-pressure—the disturbing factor is independent of the action of CHCl_3 .

Thus, the ultimate cause of fall of blood-pressure may be some kind of CHCl_3 -action, and the factor which intervenes and influences it may be, directly or indirectly, connected with some kind of CHCl_3 -action. Again, the cause of fall of blood-pressure may be independent of CHCl_3 -action, and the intervening factor which complicates the action of the heart may also be independent of CHCl_3 -action. Thirdly, the cause of fall of blood-pressure may be independent of CHCl_3 -action, but the intervening factor which complicates it may be, directly or indirectly, associated with some kind of CHCl_3 -action. It will be necessary, therefore, in determining the relation between CHCl_3 -action, considered physiologically, and the heart, to exclude all simple instances of pulse-disappearance, which proceed from independent sources, and in the case of complex instances to define the part which CHCl_3 plays in their production—the seat of its operation, and the particular kind of its action.

In CHCl_3 -anæsthesia, the frequency of the pulse is at first slightly increased, but it tends to become accelerated after an interval of stability, and the tendency is progressive—*i.e.*,

the greater the duration of anæsthesia, the greater the frequency of the pulse. This variation of the pulse, however, is invariably preceded by increased frequency of the respiration. And it is directly proportioned to the degree of the latter. Consequently, in anæsthesia, there is no direct physiological relation between CHCl_3 and the action of the heart. But if it be objected that there is some nutritional interference with its function, by reason that a foreign body or its products are circulating in and affecting the blood, the answer to the objection is that that interference is reduced, in the circumstances, to a minimum; and besides, it is known that the cardiac muscle possesses an extraordinary degree of resistance against changes in the constitution of the blood.

In CHCl_3 -narcosis, the negative and physiological actions have to be differentiated. The tension of the pulse is increased, while its frequency is diminished. And as the degree of narcotic action tends to increase, so does the tension of the pulse tend to increase, and its frequency to diminish. If the degree of narcotic action be increased beyond a certain limit, or if the initial overdose be continued for a sufficient period of time, the tension of

the pulse will be progressively increased, and the frequency progressively reduced, up to a point when the latter is increased for a short interval, but irregularly, and accompanied by diminished tension, after which it rapidly declines and disappears. If, now, at any stage of its increased tension, the action of CHCl_3 be withdrawn, the pulse will progressively return to its normal condition.

The abnormal condition which invariably accompanies plus tension of the pulse in CHCl_3 -narcosis is distension of the pulmonic artery, the origin of which is either mechanical obstruction in the air-way, or a diminution in the volume of air below a certain degree in the CHCl_3 -air atmosphere. But the influence of the former is excluded by maintaining the base of the tongue in its normal position, in the induction of simple CHCl_3 -narcosis, in which the whole of the abnormal result on the pulse will proceed from the displacement of air consequently upon the evaporation of CHCl_3 —*i.e.*, from its negative action. The phenomena, therefore, which are presented by the pulse in CHCl_3 -narcosis are explained not by a positive effect of CHCl_3 on the heart, but by its negative action which indirectly affects the action of the heart, through its direct result—*viz.*, distension

of the pulmonic artery becoming the cause of distension of the right ventricle. But the argument against the direct action of CHCl_3 on the heart, if it be assumed that it may accompany its negative action, is supported by the following facts: 1, the mode of disappearance of the pulse is invariably rapid in CHCl_3 -narcosis, and it precisely conforms to the mode of its disappearance, when distension of the pulmonic artery is produced by a neutral agent; 2, if CHCl_3 exercise a direct influence on the heart, there should be a manifestation of it in its weakened contractions immediately after the reappearance of the pulse on the occasion of its failure. But on the contrary, after the removal of the abnormal condition, which has led to the temporary loss of its function, the heart rapidly resumes its normal power of contracting.

But if it be shown that CHCl_3 cannot possibly possess any direct influence over the heart, it will necessarily follow that the actual condition of the latter, whether normal or abnormal, is a matter of no moment before its administration. That applies, however, only to its physiological action. For the heart may be affected indirectly by the negative action of CHCl_3 . Such a consequence, however, is not necessary; it does not appear in

anæsthesia. But when it is present, as in CHCl_3 narcosis, an increased amount of work will be thrown upon the heart. In such a contingency the initial power of the heart will play an important part in determining the incidence of syncope. Thus, if the cardiac strength be less than the normal, the heart will tend to fail early in its endeavour to withstand increased pressure in its right ventricle. By removing the negative action of CHCl_3 —*i.e.*, by reducing the state of narcosis to that of anæsthesia—the action of the heart will return to the normal. The abnormal conditions which surround the cardiac action and determine its failure have been made to disappear.

§ 92. *Relationship between CHCl_3 -action and muscle.* The negative and physical actions of CHCl_3 are both associated, in certain circumstances, with muscle-rigidity. This abnormal phenomenon invariably disappears when 1, the CHCl_3 -air atmosphere is replaced by air; and, 2, the air-way is rendered normally patent. It will be necessary, therefore, to exclude this form of muscle-phenomenon from the purely physiological part of the inquiry.

The muscles are in a condition of relaxation on the induction of anæsthesia, but apparently their tone is not affected. In the course of

anæsthesia, however, there is a tendency to diminishment of tone. Thus, the application of the same degree of intensity of the stimulus will be followed by a less degree of contraction at the end of 30'; and the sensitiveness of the muscles will become further diminished as the duration of anæsthesia is prolonged, so that after the lapse of 2° the response of the muscle will not only be tardy but also limited to the seat of stimulation, instead of affecting the whole muscle. But as the degree of CHCl_3 -action is progressively reduced, with the object of maintaining a constant state of anæsthesia, it will be perceived that a progressively diminishing degree of intensity of the cause is associated with a progressively increasing degree of one of its results. A variation is consequently to be sought in one of the conditions which affect muscle-vitality.

In narcosis the same tendency is perceptible, but its manifestation occurs earlier than in the case of anæsthesia. In the course of narcosis, maintained at the same degree, diminishment of muscle-tone progressively increases, and at a more rapid rate than that in anæsthesia. But the degree of minus-tone is not the same for all degrees of the state of narcosis. For this characteristic difference is presented. Given initial

normal muscles, the greater the degree of the narcotic action of CHCl_3 , the less will be the sensitiveness of muscles to local stimulation. Thus, the same degree of intensity of a stimulus will, in a low degree of narcosis, be followed by a late and limited range of muscle-contraction, while in the higher degrees of narcosis it will induce but a faint movement, or perhaps none at all.

When the initial condition of the muscles is abnormal—*i.e.*, their vitality is diminished—it is found that while the same results are produced as in normal muscles, yet they appear earlier than in the latter, both in anæsthesia and narcosis.

The factors, then, which are concerned in the causation of muscle-phenomena, considered from the physiological standpoint, are the following: 1, the degree of CHCl_3 -action; 2, its duration; and, 3, the initial condition of the muscles.

The condition of muscular relaxation at the onset of anæsthesia is explained by the suspension of the functions of the cerebral centres. Consequently it will be secondarily related to the physiological action of CHCl_3 .

But the suspension of the functions of the cerebral centres is not equal to explain loss

of muscle-tone. It follows, therefore, that that phenomenon is primarily related to physiological action, and the evidence will point to the conclusion that it is indirectly caused by that action.

Thus, on the withdrawal of the CHCl_3 -air atmosphere, no matter what the circumstances may be at the time, the muscles begin to recover their natural tone, which they reach after an interval that is shorter in anæsthesia than in narcosis, and in anæsthesia is shorter in instances of short than in those of longer duration. For example: anæsthesia was induced in a normal adult, and maintained for a period of 10'. The return to consciousness occupied 3', and 2' afterwards the patient was able to walk from one room to another without any assistance. The effect upon muscle-tone was by inference very slight, because it was so quickly removed. And the principal factor in promoting recovery from the results of CHCl_3 -action is the patency of the air-way; for, when it is maintained normally patent, the return to consciousness is effected in the quickest possible time.

It would appear, then, that there is a causal factor that exercises an evanescent influence on the function, and therefore on the nutrition, of the muscles. For, as has been observed, the

intensity of the result begins to diminish as soon as the CHCl_3 -air atmosphere is withdrawn; and in order to maintain it, it is necessary to continue the administration of CHCl_3 .

Now the muscles are known to be sensitive to variations in the proportion of oxygen in the blood. In narcosis the $-\text{OXy}$ -factor is present. And it might be objected that as the negative action of CHCl_3 produces deoxygenation, and as it is inseparably associated with a state of narcosis, a cause is present and operating which will account for the diminishment of muscle-tone. But does the shortage of oxygen from this source explain the whole of the result? The following comparative investigation will show that it cannot. If the same degree of deoxygenation, as in CHCl_3 -narcosis, be induced by a neutral agent, it is found that while in the latter there is a greater degree of respiratory obstruction—*i.e.*, a higher degree of negative action—in the former there is a greater degree of muscle-change. But in anæsthesia, in which the negative action of CHCl_3 is efficiently counteracted, the same result appears. The objection, therefore, is demonstrated to be groundless.

The fact that $-\text{OXy}$ is the sole factor in the

causation of loss of muscle-tone appears from the following considerations: when the blood is deoxygenated, and the action of CHCl_3 is continued, the rate of diminishment of muscle-tone is more rapid than that which obtains in anæsthesia; when the state of narcosis is reduced to anæsthesia by diminishing the proportion of CHCl_3 in the CHCl_3 -air atmosphere, the change in the colour of the blood is invariably associated with a change in the degree of muscle-sensitiveness; as the blood becomes more and more reoxygenated, so do the muscles become more and more sensitive, becoming normally so when the blood has been rendered normal; when the blood is again deoxygenated, by increasing the CHCl_3 -constituents, muscle-sensitiveness is diminished, and as the degree of deoxygenation is increased, so does the degree of loss of muscle-tone become increased.

The result on the muscles—viz., a diminishment of their tone—is thus shown to be caused by $-\text{OXY}$. And the principal cause of shortage of oxygen, where, as in narcosis, these are more than one, is traced to the physiological action of CHCl_3 . The $-\text{OXY}$ -factor is consequently intermediate between that action and the loss of muscle-tone which is associated with it.

§ 93. *The relationship between CHCl_3 -action*

and the pupil.—The study of the variations which are presented by the pupil during the administration of CHCl_3 certainly forms the most interesting, if it be not the most important, part of the problem.

The action of CHCl_3 is not associated with any one condition of the pupil, but different degrees of action are accompanied by different sizes of it. Nor does the degree of dilatation, which corresponds to a given degree of CHCl_3 -action, remain constant throughout the continuance of it; for, after a certain period, the size of the pupil is increased, and the tendency is manifested at the end of subsequent periods, which, however, become shorter in length. In these circumstances the mode of onset of dilatation is gradual. But instances occur in which the pupil becomes fully dilated, rapidly or suddenly, in the course of the ordinary administration of CHCl_3 . The circumstances in which it does so are different from those which accompany its gradual dilatation. They are, 1, sudden or rapid fall of blood-pressure when it is of sufficient intensity; and, 2, some forms of respiratory arrest. Now, the action of CHCl_3 may be primarily associated with one form of fall of blood-pressure, and with two forms of arrest of the action of the respiratory machine.

Thus, it will be perceived that the relationship between the pupil and CHCl_3 -action is intricate: it may be primary or secondary in simple instances, and, in complex ones, it may be both.

It will be necessary, in order to elucidate this part of the problem, to classify the different varieties of the pupil which may occur in the ordinary administration of CHCl_3 .

The pupil is contracted or pin-point in anæsthesia. And if the degree of CHCl_3 -action be progressively diminished, that condition of it will be rendered constant. But in the course of CHCl_3 -anæsthesia, mechanical obstruction may intervene and cause duskiness. If the degree of obstruction be moderate, the pupil will preserve its contracted condition for a period, after which it will gradually dilate. But if the degree of obstruction be such as to embarrass the action of the respiratory machine, the pupil will begin to dilate when the act of inspiration is temporarily interrupted, and will immediately afterwards become rapidly dilated to the full while preserving its sensitiveness. On the removal of the source of obstruction it becomes rapidly contracted to the normal, when no relative blood-overdose is present, and to that degree of dilatation which corresponds to the degree of relative narcosis, when the

latter accompanies this form of respiratory arrest. The irregularity in the attitude of the pupil, on the recovery from inaction of the respiratory machine, is explained by the fact that different degrees of the abnormal condition of the blood may antecede the onset of arrest. Thus, the effect of CHCl_3 -action on the blood may be either anæsthetic or narcotic before its occurrence. But the recovery of the function of the respiratory machine is not necessarily followed by the immediate return of the blood to the normal. And, in the case of narcosis, an interval will elapse before the blood becomes normally oxygenated. Seeing that the abnormal condition of the blood in CHCl_3 -narcosis is invariably accompanied by dilatation of the pupil, and that variations of degree of the former are directly proportioned to variations in size of the latter, it will follow from the causal nexus which exists between them that, if the condition of the blood be exactly alike in any two instances of temporary respiratory arrest, the attitude of the pupil will be the same in both on the recovery of respiration.

In CHCl_3 -narcosis the pupil is dilated; but there is no uniform degree of dilatation. The degree of dilatation varies with, and is directly proportioned to, the degree of narcotic action.

The rapidity with which dilatation takes place is greater or less, according to the greater or less rate of increase of the CHCl_3 -constituent in the CHCl_3 -air atmosphere. Thus, from the condition of normal contraction, it may become rapidly dilated to one-half within 45" by increasing sufficiently the proportion of CHCl_3 . But the mode of dilatation of the pupil in CHCl_3 -narcosis is gradual, as compared with its sudden dilatation in other circumstances—*e.g.*, the immediate dilatation to the full associated with severe fall of blood-pressure.

In the course of the dilatation of the pupil from the narcotic action of CHCl_3 , a characteristic is developed which separates it from all the other forms of dilatation which may occur in ordinary practice. It loses its sensitiveness to the action of light. But the loss of muscle-tone is effected not immediately, but progressively. For while in the lower degrees of dilatation the pupil reacts quickly but less powerfully than normally, it is found that as the size of the pupil is made to increase, its reaction to light is delayed and its contraction reduced in degree; so that when it is fully dilated the stimulus of light is not followed by any reaction at all. This tendency of the pupil to become more dilated and sluggish with

an increase in the degree of CHCl_3 -narcosis, and the fact that there is an inverse proportion between the degree of dilatation and that of sensitiveness, will help to explain both the causation and mechanism of the dilatation of the pupil in CHCl_3 -narcosis.

The degree of narcotic action being maintained constant, the pupil will present at the end of a certain period an increase of dilatation, thus manifesting the same tendency as appears in anæsthesia. And in all instances of the "sluggish" pupil, its reduction to the normally contracted state is effected either by progressively increasing the proportion of air in the CHCl_3 -air atmosphere, in which case the return to the normal will be gradual, or by removing the influence of CHCl_3 altogether, when the return will be rapid. The pupil, after being contracted from the abnormal condition of dilatation, does not exhibit any impairment of its sensitiveness, a fact which shows that the influence of CHCl_3 upon it has not been (relatively) permanent. And the relationship between the reoxygenation of the blood and the reduction of the dilated pupil—if oxygenation is retarded, contraction is delayed, and if the blood is continuously oxygenated, contraction is progressive—will be found to have an important bearing

upon the nature of the physiological action of CHCl_3 .

Dilatation of the pupil is always associated with fall of blood-pressure when of sufficient intensity. It may or may not be associated with arrest of the action of the respiratory machine; thus it does not occur in voluntary arrest when the antecedent conditions have been normal, but it invariably occurs in functional arrest, and in mechanical arrest, when it is accompanied by certain abnormal conditions of the circulatory system. It would appear, therefore, that the respiratory centre is not directly connected with the pupil: 1, functional arrest of its activity is necessarily followed by secondary fall of blood-pressure; and 2, primary fall of blood-pressure is associated with dilatation of the pupil. In all these instances of dilated pupil its sensitiveness to light is normally preserved. And this sensitive character forms the readiest means of differentiating it from the sluggish dilated pupil of CHCl_3 -narcosis.

But there is another group of the sensitive pupil which is characteristic of abnormal anæsthesia. The factors which are associated with it are—1, extreme emaciation; 2, high fever; and, 3, long-continued pain. All of them tend to exercise a prejudicial influence on nutrition.

Consequently the condition of the iris will be more sensitive than normally to alterations temporarily induced in the constitution of the blood. This form of the sensitive pupil tends to become contracted in the course of the anæsthetic action of CHCl_3 , but its return to the normal, though progressive, is gradual. It would appear, therefore, that the action of CHCl_3 affects unduly the nutrition of the iris when its condition is initially unstable. And the fact that the iris tends to become accustomed to the interference which is produced in its nutritional surroundings by the initial action of CHCl_3 , may help to elucidate the nature of that action.

If the degree of CHCl_3 -action is maintained constant, the size of the pupil tends to increase. But the size of the pupil can be kept constant by progressively diminishing the degree of action. Thus, in the course of the administration, the same result—*e.g.*, the contracted pupil of normal anæsthesia—is associated with a less quantity of the agent which is concerned in its production. On the other hand, the same quantity of the agent is, in narcosis, associated with different degrees of dilatation of the pupil at different times. The inference, therefore, is drawn that the relationship between CHCl_3 -action and the

pupil is not a direct one, but that a variation takes place in some condition of the iris that opposes less resistance to it. And the following facts support this view: 1, In instances of more than the ordinary amount of fear which is presented before the administration, the pupil, which is widely dilated, does not conform to the series of changes that are presented in normal examples. Thus at the onset of automatic respiration the pupil remains dilated, and continues so for a few seconds, after which it rapidly contracts. 2, Respiratory inhibition may intervene and complicate the state of normal anæsthesia. When it does so, the pupil becomes dilated during its progress and preserves its sensitiveness. But the degree of CHCl_3 -action is less than it was at the commencement of anæsthesia, and has been reduced (below the normal for the particular stage in which the complication appears) in order to meet the requirements of the abnormal state of the respiratory machine. An influence superior to that of CHCl_3 operates to prevent the production of the maintenance of the normally contracted pupil. But if the degree of CHCl_3 -action be higher—*i.e.*, a moderate degree of narcosis is present, and a fall of blood-pressure takes place—the pupil will undergo suddenly an increase of dilatation. Thus, though

the size of the pupil is of first-rate practical importance in the administration of CHCl_3 , yet it is not of fundamental importance in the investigation of the nature of the physiological action of CHCl_3 . But its significance lies in its being one of the means which lead to the isolation of the direct effect of that action.

The factor which intervenes and complicates the result of CHCl_3 -action on the pupil may or may not derive from CHCl_3 itself. Thus the occurrence of sudden dilatation during constant anæsthesia, and of the sudden increase of dilatation during the course of a constant but moderate degree of narcotic action, will point to the presence and operancy of some agent which is independent of CHCl_3 , but is acting collaterally and simultaneously with it. But in respect of the instance of the gradual dilatation of the pupil in CHCl_3 -narcosis, the evidence points to the origin of the factor as being in a product of CHCl_3 -action.

With the help of the foregoing data, it is possible to proceed to the consideration of the mechanism of the dilatation of the pupil.

The pupil is contracted in CHCl_3 -anæsthesia and in sleep, which is the lowest degree of unconsciousness. But the pupil is dilated in CHCl_3 -narcosis, in which the degree of result

upon the cerebral centres is inferred to be greater than that which exists in anæsthesia, on the ground that, given the normal patency of the air-way, consciousness is recovered more quickly in the latter than in the former. Now, there is a direct proportion between the degree of narcosis—*i.e.*, the degree of abnormality of the cerebral centres—and the length of time which is required for the recovery of consciousness. And inasmuch as that variation in the abnormal condition of the cerebral centres is accompanied by a corresponding variation in size of the pupil,—for as the former is greater or less, so is the latter greater or less,—it might be argued that a causal nexus exists between them, and therefore that the degree of the abnormal condition of the cerebral centres will determine the degree of dilatation of the pupil. The argument, however, is rebutted by the following facts: 1, in opium-narcosis, suspension of the cerebral functions is associated with a contracted pupil, while in a similar degree of CHCl_3 -narcosis, as measured by the degree of discoloration of the blood, the pupil is dilated, but the difference might be explained by the less or greater rapidity with which deoxygenation takes place; 2, in the state of unconsciousness, induced by cerebral hæmorrhage, the condition

of the pupil is not constant, but varies according to the site of the hæmorrhage. Thus the pupil is contracted in hæmorrhage into the Pons; dilated when it occurs in the island of Reil. It will be necessary, however, to exclude in each particular instance interference with the venous circulation of the eye.

It would appear, therefore, that the actual condition of the pupil is independent of the abnormal condition of the cerebral centres. But it is possible that both the pupil and the cerebral centres may be affected by a common factor. Supposing that they are so, the direct proportion between their variations in different degrees of CHCl_3 -narcosis will be explained.

Now, the factors which present variations, and which, consequently, may possess an influence in the production of the dilated pupil, are these: 1, the circulation; and 2, the condition of the blood. But the state of the circulation is practically normal in sleep and in normal CHCl_3 -anæsthesia, in both which the pupil is contracted, while in the state of collapse, induced by loss of blood, the pupil is widely dilated. Again, the state of unconsciousness may be associated with minus arterial tension and a dilated pupil (reflex stimulation of the vaso-motor centre occurring during CHCl_3 -

anæsthesia); or with plus arterial tension and a contracted pupil.

Different variations of the circulation are thus seen to be accompanied by different conditions of the pupil. If, then, a causal nexus exists between them, the same variation of the antecedent phenomenon—viz., the same change of blood-pressure—will invariably be followed by the same variation of the consequent—viz., by the same change in the size of the pupil—unless some particular and occasional factor is demonstrated to be present and to prevent it. But in the case of plus-tension the pupil may be dilated as in CHCl_3 -narcosis, or contracted as in mixed unconsciousness, produced by the anæsthetic degree of CHCl_3 -action and mechanical obstruction. And in that of minus-tension the pupil also may be dilated as in vaso-motor depression, or contracted as in respiratory inhibition. It must be noted, however, that, 1, in CHCl_3 -narcosis as tension increases so does the degree of dilatation of the pupil increase, and as the degree of plus-tension is reduced so does the degree of dilatation become less; and, 2, varying degrees of minus-tension below a given standard are associated with varying degrees of dilatation, so that the greater the fall of blood-pressure the larger is the size of the pupil.

Unless, therefore, some particular factor can be proved to exert a contrary influence on the condition of the pupil, in certain instances no definite conclusion respecting it can be drawn from the comparative study of variations of tension.

The condition of the blood may or may not be normal when the pupil is dilated. In the case of the dilated pupil, which follows upon reflex stimulation of the vaso-motor centre, the blood is normal. But in that of CHCl_3 -narcosis the blood is invariably discoloured. While, however, its sensitiveness is unaffected in the former, in the latter it is impaired. It will be necessary, therefore, to inquire into the cause of the sluggishness of the pupil.

Muscle-tissue is especially sensitive to variations in the proportion of oxygen in the blood. Now, in CHCl_3 -narcosis there is evidence of a diminishment of oxygen supplied by the discoloration of the blood. And from the fact that the reoxygenation of the blood is effected gradually, as compared with the rate at which it takes place, when a neutral agent is the source of deoxygenation, the inference may be drawn that the blood is affected differently in CHCl_3 -narcosis. But as the blood eventually becomes normally oxygenated without the manifestation

of any impairment of any of its constituents, it would appear that there is another source of deoxygenation than that supplied by the negative sphere of the narcotic action of CHCl_3 .

The minus oxygen-factor, as a cause of diminishment of muscle-tone, will explain the sluggishness of the pupil to the action of light. If, then, it can be demonstrated that in a certain group of instances, a variation of the $-\text{OXY}$ -factor is invariably followed by a corresponding variation in the degree of sluggishness, and that when the cause ceases to operate—*i.e.*, the blood is normally oxygenated, the whole of the result will disappear—*i.e.*, the pupil becomes normally sensitive, the conclusions will inevitably follow, 1, that a causal nexus exists between the antecedent—*i.e.*, $-\text{OXY}$ and the consequent—*i.e.*, the degree of sluggishness; and, 2, that no other cause besides $-\text{OXY}$ is present to interfere with its effect on the pupil. But such can be demonstrated in the case of the dilated sluggish pupil of CHCl_3 -narcosis.

A comparison being now instituted between the dilated pupil of CHCl_3 -narcosis on the one hand and the contracted pupil of mixed unconsciousness—*i.e.*, CHCl_3 -anæsthesia complicated by mechanical obstruction—and of opium-narcosis on the other, it will be perceived that the

circumstances in which the $-\text{OXy}$ -factor, which is common to them, operates, present the following differences: I. The degree of intensity of the causal factor is greater in CHCl_3 and in opium-narcosis than in that of mixed unconsciousness, on the supposition that the duration of mechanical obstruction complicating normal CHCl_3 -anæsthesia is limited to the stage of the contracted pupil; for if it be extended beyond that stage the reduced degree of CHCl_3 -action will become relatively narcotic, and will consequently be accompanied by dilatation. In mixed unconsciousness, therefore, the effect of $-\text{OXy}$ upon the iris is assumed (for the present) to be insufficient to impair its nutrition. It therefore remains in the condition of natural repose. II. But the pupil is contracted in opium-narcosis, in which there is a greater degree of deoxygenation than in the example of mixed unconsciousness, which has just been considered. It cannot be argued, however, that that difference in the degree of the intensity of the $-\text{OXy}$ -factor is sufficient to affect the tone of the iris. For the muscles possess a power of resistance which is offered against encroachments upon their oxygen-supply; and before that is overcome it is essential that the antagonistic cause shall reach the necessary degree

of intensity. Assuming that there is another cause of deoxygenation than that of defective aeration, it is conceivable that it may be present in different degrees of intensity. Thus, in opium-narcosis, the degree of deoxygenation, though sufficient to cause unconsciousness, may conceivably be insufficient to cause the requisite degree of effect upon the iris, which is followed by the dilatation of the pupil. But in CHCl_3 -narcosis the pupil is dilated. The difference in the size of the pupil will, therefore, point to the circumstances in which the agents respectively operate. It is possible that one of them exercises a greater influence on the volume of oxygen in the blood than the other. It is also possible that the rate of their absorption, and consequently the rapidity with which they come into action, may differ. Now it is known that, under favourable conditions, CHCl_3 -vapour is quickly absorbed into the blood. On the other hand, an interruption to the progress of the action of opium may be effected by judicious treatment; and during it signs of returning consciousness may be manifested which would point to a progressive rather than an instantaneous absorption of the whole of the agent. The rapidity with which the whole of the agent comes into operation will explain why the

pupil is contracted in opium and dilated in CHCl_3 -narcosis, loss of muscle-tone being more quickly effected in the latter than in the former. But it is to be observed that, 1, the pupil does not continue contracted throughout the whole period of opium-narcosis, but begins to dilate and progressively dilates during the later stages of it; and, 2, that in mixed-unconsciousness, when the degree of CHCl_3 -action becomes relatively excessive, the pupil dilates. Both these forms of dilatation are accompanied by sluggishness. The inference, therefore, will be that a tendency, and probably the same tendency, to dilatation of the pupil is created by the agents in question, and that in certain circumstances it becomes uncounteracted. Now, the $-\text{OXY}$ -factor is known to possess that tendency, and the favourable circumstance to its manifestation can be demonstrated to exist in both the above instances—viz., an increase in the degree of deoxygenation—which is inferred from the increased discoloration of the blood that appears in them.

The mechanism of the dilatation of the sluggish dilated pupil of CHCl_3 and its congeners is thus explained. And it will be perceived that arterial tension does not play the most important part in it as it would do if the iris

were composed of blood-vessels alone. For if that were the case, increased tension, which invariably accompanies the narcotic degree of CHCl_3 -action, would necessarily be followed by contraction of the pupil. The fact, however, is that the pupil is dilated and sluggish in CHCl_3 -narcosis. If, therefore, plus-tension tends to contract the pupil, it follows that that tendency is opposed and overcome by another tendency, which is the product of CHCl_3 -action. And thus a reason is adduced for the muscular structure of the iris.

But dilatation of the pupil may occur without any antecedent change in the condition of the blood. Consequently, it would seem that the explanation which is satisfactory for one form of dilatation is not for another. The question, then, is presented, Is the mechanism of dilatation different in different forms, or is it fundamentally the same in all forms?—*i.e.*, the same effect upon the iris is produced, though in different ways by different agents. For the sake of clearness, the action of artificial agents, applied externally, is for the present excluded.

When the pupil dilates during the normal condition of the blood, it invariably preserves its sensitiveness. Its mode of onset is either rapid or sudden—*i.e.*, it reaches its actual degree

of dilatation within a space of time which cannot be measured. The circumstances under which it dilates are different, and are as follows : 1, returning consciousness from normal anæsthesia ; 2, extreme degrees of the state of emotion ; 3, reflex stimulation of the vasomotor centre ; and 4, sympathetic stimulation of that centre, consequent upon functional arrest of the action of the respiratory centre.

If, now, a comparison be made between these factors in so far as regards the condition of arterial tension, it will be seen that, in returning consciousness, the circulation is practically normal, and that the muscles exchange their natural condition of relaxation for one of normal tone—*i.e.*, they will become obedient to the new conditions which govern them ; while in all the other examples there is a fall of blood-pressure, accompanied by muscle-collapse. In the former there is no interference with the blood-supply of the iris ; consequently, the dilatation of the pupil is a normal phenomenon ; but in the latter there is interference with the nutrition of the muscles, consequently their function is impaired : the dilatation of the pupil occurring under these abnormal circumstances will therefore be abnormal.

But minus arterial tension alone will not

explain the dilatation of the pupil in those circumstances. For if it were the sole cause, the same variation in the degree of its intensity would invariably be followed by the same change of size of the pupil. But the pupil is contracted during respiratory inhibition, complicating the anæsthetic degree of CHCl_3 -action, and consequently is associated with secondary fall of blood-pressure. And as no tendency can be isolated which prevents the (assumed) effect of minus-tension, another reason may be adduced in favour of the muscle of the iris.

The study of minus arterial tension, however, affords the means of elucidating in part the mechanism of dilatation. Thus, a severe fall of blood-pressure, associated with the disappearance of the pulse, is immediately followed by dilatation of the pupil. But when tension is raised (and there is supposed to be no interruption to the natural progress of vaso-motor complication occurring during normal anæsthesia) the pupil does not contract gradually, but rapidly reaches the normal degree of contraction before the pulse is perceptible at the wrist, and therefore before the reappearance of the normal degree of arterial tension. Thus, in the rise of arterial tension from a minimum, as in its decline, there is no invariable relation

between its degrees and the size of the pupil. But when tension is gradually reduced from a degree higher than the normal, as in CHCl_3 -narcosis, in which the blood is invariably deoxygenated, the size of the pupil gradually diminishes. And it also increases as the degree of tension is made to increase. But, though in these circumstances there is demonstrated to be a direct proportion between the variation of tension and that in the size of the pupil, yet it does not occur in all circumstances of increased tension. Consequently it is not an invariable relationship, but is limited to particular circumstances, amongst which is the narcotic degree of the action of CHCl_3 . The conclusion, therefore, will follow that a factor is present which is independent of arterial tension, but which may be affected by it in certain circumstances—*e.g.*, severe degrees of all of blood-pressure. For the degree of tension determines the amount of blood supplied to the iris. Minus variations in the amount of blood tend to impair its nutrition. And its actual condition at any given time, as determined by its nutritional surroundings, determines its tone, and consequently the manner in which it performs its function.

The two groups of the dilated pupil—the

sensitive and the sluggish—are thus connected by means of a common factor. In the former, the invariable antecedent is diminishment of blood—and therefore of oxygen—supply, which, however, has to be rapidly induced. In the latter it is interference with the nutrition of the iris, produced by the abnormal condition of the blood, the abnormality being restricted solely to one constituent of it—viz., diminishment of oxygen. But the circumstances in which the —OXY antecedent operates are different. Thus, in the one, immediate and severe fall of blood-pressure is followed by a complete but temporary abstraction of oxygen from the iris, a condition which is known to determine the temporary collapse of muscle-tissue; in the other, the abstraction of oxygen is effected more or less gradually. But when a normal muscle is deprived of its blood-supply it does not forthwith lose its sensitiveness, but it responds normally to local stimulation, because its nutrition has not been antecedently impaired. On the other hand, when its nutrition has been continuously and adversely affected, as by the removal of oxygen in the blood, its condition becomes abnormal, and this abnormal condition is known to influence the result of stimulation. Now, the abnormal condition pro-

duced by $-\text{OXy}$ does not continue after the replacement of the normal volume in the blood ; but with the increase of oxygen it progressively disappears, so that when the blood becomes normally oxygenated the normal condition of the muscle reappears.

Fall of blood-pressure is effected by different agents : ideo-motor reflex action, reflex stimulation of the vaso-motor centre, and external hæmorrhage. Deoxygenation is also effected by different agencies : defective aeration and the abstraction of oxygen from the blood. But not all degrees of deoxygenation nor all degrees of fall of blood-pressure are associated with dilatation of the pupil. The degree of deoxygenation has to reach a given limit before the pupil begins to dilate, and in the course of its dilatation an additional abnormality appears in the reduction of its sensitiveness. Now the $-\text{OXy}$ -factor, by causing loss of muscle-tone, explains both those characters of the pupil. And blood-pressure has to fall below a certain degree before it is accompanied by dilatation of the pupil. It will be necessary, therefore, to distinguish between the circumstances which affect the operation of the $-\text{OXy}$ -factor on different occasions, in order to explain the differences in conduct which are presented by the

dilating and dilated pupil. For example, the pupil may be dilated to one-half at the end of 10' in CHCl_3 -narcosis; the degree of intensity of the $-\text{OXY}$ -factor is moderate and has operated during a comparatively short period of time. But the pupil remains in a normal condition of contraction for 2° in CHCl_3 -anæsthesia in which the $-\text{OXY}$ -factor is present in a degree of intensity that is insufficient to affect to the requisite extent the nutrition of the iris.

It is necessary to explain the causation of the dilated sensitive pupil when it occurs in the course of CHCl_3 -administration. The circumstances under which it appears are different. Thus, it may occur suddenly during the progress of normal CHCl_3 -anæsthesia. When it does so it is invariably accompanied by sudden fall of blood-pressure. And a sudden fall of blood-pressure, below a given degree, is followed by sudden collapse of the iris. In this group the physiological action of CHCl_3 is not causally connected with the dilatation of the pupil. But in abnormal CHCl_3 -anæsthesia, the pupil is dilated and sensitive at the onset of automatic respiration, though it tends to become subsequently contracted. The initial condition of the iris is, however, abnormal—*i.e.*, it has become unstable as the consequence of inter-

ference with its nutritional surroundings. The physiological action of CHCl_3 will, in these circumstances, be associated with a relatively undue degree of nutritional disturbance, and the instability of the iris will be rapidly increased as the natural result of the change that has been rapidly induced in its abnormal surrounding conditions. A factor is thus isolated to explain the dilatation of the pupil. But it will eventually become contracted, and its progress towards the normally contracted state is gradual, occupying different periods of time in different examples, the shortest being 10', the longest 25'. The resisting power of the iris is less than the normal. But an abnormal iris, just like a normal one, will present a degree of resistance against encroachments on its vitality, though it will be less than that opposed by the latter. And just as normal tissues tend to adapt themselves to a constant change of their surroundings, so do abnormal ones, but it takes a longer time for the latter to reach the condition of equilibrium. The pupil becomes contracted because the initial effect of CHCl_3 is, in course of time, completely counteracted by the iris.

§ 94. *The relation between CHCl_3 and the blood.*
— CHCl_3 is absorbed into the blood as a vapour,

and is assumed to circulate in it. But it loses its characteristic odour in the process, for no trace of it can be detected in blood issuing from a wound during CHCl_3 -unconsciousness, even when the degree of narcosis is high. The inference, therefore, is that CHCl_3 undergoes some change when in contact with the blood, and that it either enters into some higher combination or into a lower one—*i.e.*, it is decomposed. The CHCl_3 -product will thus take the place of CHCl_3 in the causation of the phenomena which have been ascribed to the latter.

There is no discoloration in anæsthesia, so far as the naked eye can determine. A certain proportion of air is displaced, but the circumstance of the increased frequency of respiration explains the occurrence of the normal aeration of the blood. Increased frequency of respiration is a known consequence of an alteration in the proportions of O_2 and CO_2 . An alteration can thus be effected within a given limit, which does not cause any perceptible change of colour.

If CHCl_3 exercises any influence on the blood, it is not directly manifested in the anæsthetic degree of its action. But because no change is connected with that particular degree of its action, it cannot be inferred that it has no

effect at all, unless it be shown that when the degree of action is increased no alteration in it is perceptible. For living tissues possess the power of accommodating themselves to changes within certain limits, without manifesting any apparent alteration of their condition. But increase the change up to the requisite degree, and an alteration of condition will become directly or indirectly obvious.

In CHCl_3 -narcosis the blood is invariably discoloured. And the degree of discoloration is directly proportioned to the degree of narcosis. It may consequently be taken as a measure of the latter. A causal nexus is thus shown to exist between CHCl_3 -action and the discoloration (or deoxygenation of the blood). But the maintenance of the normal patency of the air-way is of the first importance in experimenting with slight differences in the degree of narcotic action, for the influence of a disturbing factor—viz., mechanical obstruction—is thereby removed.

There is a greater displacement of air with the narcotic than with the anæsthetic degree of CHCl_3 -action. And in the former, as the proportion of CHCl_3 increases, so does that of air diminish. Defective aeration, therefore, will explain the relation between the narcotic action

of CHCl_3 and the blood. For a diminishment of oxygen below a certain limit is accompanied by discoloration, and the greater the degree of the former the greater will be the degree of the latter. But defective aeration is the consequence of the negative action of CHCl_3 ; and apparently it satisfies all the requirements respecting the blood.

Besides the discoloration of the blood, however, other phenomena characterise the state of narcosis; for example, the pupil is more or less dilated and more or less sluggish. And further, as the degree of narcotic action is maintained constant, a tendency appears to a variation of results; the blood becomes progressively darker, and the degree of dilatation of the pupil progressively increases. Does the causal factor, which has just been isolated, explain these variations? The following considerations are necessary in order to decide the question.

The anæsthetic proportion of CHCl_3 is not constant for all conditions, but varies with the quantity and quality of the blood. Thus, the same amount of displaced air which is associated in the normal condition of the blood with no discoloration, is in the anæmic associated with its discoloration.

The higher the degree of the overdose, the

more rapid is the rate of increase in the degree of discoloration during the narcotic action of CHCl_3 . But by progressively diminishing the proportion of CHCl_3 , the degree of narcosis is maintained constant. Thus, with an increase in the proportion of air, the discoloured blood remains the same in degree of intensity. It follows, therefore, that some causal factor other than the negative action of CHCl_3 is present, and that it tends to counteract a reduction of its degree.

Does, then, the blood become less resistant in regard to one of its constituents ?

The same amount of CHCl_3 is followed by the same quantity of physiological effect. Now, this, in the instance of anæsthesia, is associated with a tendency to increased frequency of respiration and to diminution of muscle-tone as well as to discoloration of the blood. It is conceivable, and therefore possible, that the blood undergoes a variation of condition which renders it less resistant to the action of CHCl_3 . In the course of the action of CHCl_3 the same degree of result is produced by a less degree of its intensity. The change which the blood undergoes is capable of being easily removed by air, as is seen in narcosis of short and in anæsthesia of long duration. And the fact that

the blood returns to the normal, as indicated by the return to the normal of the frequency of respiration, proves that the change which is effected in it is not followed by any enduring result.

The introduction of this factor—viz., a variation of the blood—leads to the explanation of the Law of Diminishing Resistance.

A constant CHCl_3 -air atmosphere is attended by increased frequency of respiration, which progressively increases, and by discoloration of the blood, the intensity of which also progressively increases in degree. Increased frequency of respiration tends to consume the reserve power of the muscles, and consequently tends to their exhaustion. The respiratory muscles, in their weakened condition, become less able to expel efficiently the relatively heavy CHCl_3 -air atmosphere; and the commencement of a respiratory overdose is favoured, which gradually increases in degree of intensity.

When a comparison is made between the results on the respiratory machine of a constant CHCl_3 -air atmosphere and of a neutral atmosphere displacing a like amount of air, the following differences are observed: 1, the tendency to disablement of the respiratory machine is manifested much earlier in the former than the

latter; 2, while the pupil tends to progressively dilate in the former, it remains contracted in the latter.

The cause of the disablement of the respiratory machine in CHCl_3 -narcosis is indirectly, not directly, due to muscle-exhaustion. For there is no immediate manifestation of actual muscle-change in anæsthesia, as there would be if CHCl_3 acted directly upon that tissue. An abnormal condition of the respiratory centre, induced directly by CHCl_3 , is excluded, by reason that its withdrawal is followed by a rapid return to the normal of the action of the respiratory machine. The discoloured—*i.e.*, the deoxygenated—condition of the blood remains, therefore, as the direct source of muscle-change. Nutritional interference, in the form of the diminishment of oxygen, will thus appear as an important factor in the explanation of the rate at which muscle-exhaustion occurs. And it may be inferred that in narcosis there is a greater diminishment of oxygen than in the instance with which it is compared, and that that is the additional factor which accounts for the differences that exist between them. In both there is deoxygenation, but the degree of it is greater in CHCl_3 -narcosis, in which state the blood is affected not only through defective aeration—*i.e.*,

the consequence of negative action—but also directly by the physiological action of CHCl_3 .

§ 95. *Summation of the data entering into the solution of the problem.*—The Law of Diminishing Resistance is partially explained by the negative and physical actions of CHCl_3 . But the fundamental basis upon which it rests is nutritional interference with the respiratory muscles. For, in the circumstances, these muscles have more than the ordinary amount of work to do. And they are supplied with blood which is not only of abnormal quality, but may also be deficient in quantity. The $-\text{OXy}$ -factor is sufficient to account for the comparatively rapid rate with which they lose their tone, the comparison being made with instances of simple defective aeration, in which the tone of the respiratory muscles does not appear to be at first appreciably affected.

The increased frequency of respiration in anæsthesia is due in some part to the displacement of air. A certain proportion of oxygen may be abstracted from the blood without producing any (appreciable) discoloration of it. The $-\text{OXy}$ -factor is the direct cause of the suspension of the functions of the cerebral centres. Different quantities of blood require the removal of different amounts of oxygen, in order to reach the

same degree of deoxygenation. Thus, the explanation is effected of the difference in the amount of CHCl_3 that is needed to produce anæsthesia in children and adults—*i.e.*, in examples which are characterised by difference in the quantitative condition of the blood.

In narcosis the degree of respiratory frequency varies directly with the degree of the narcotic action of CHCl_3 . The variation is partially explained by the difference in the amount of air displaced by CHCl_3 -vapour in the CHCl_3 -air atmosphere. But the same difficulty is presented as in the state of anæsthesia. It is removed by introducing a second source of deoxygenation—*viz.*, the removal of oxygen by the direct action of CHCl_3 on the blood. And it would seem that the respiratory centre is alone affected by variations of the OXY -constituent of the blood.

The progressive diminution of muscle-tone (excluding the circumstances of exposure and the artificial interference with blood-supply) is explained by the constant effect of less than the normal supply of oxygen to the muscles. Its rate of increase is greater in narcosis, where the abstraction of oxygen is greater, and less in anæsthesia, where it is less. And as in the instance of respiratory frequency, the negative ac-

tion of CHCl_3 is equal to explain some part of the result, but not the whole of it. It has already been shown that the dilated sluggish pupil, which is characteristic of CHCl_3 -narcosis, cannot be explained by negative action, and that it provides evidence of the presence of an additional -Oxy-factor.

The reoxygenation of the blood in CHCl_3 -narcosis is effected more slowly than in the instances of mechanical obstruction, and of a neutral -Oxy-atmosphere. The inference drawn from this circumstance is either that a larger volume of oxygen is withdrawn, or that a causal factor is present and prevents oxygenation until such time as it is itself destroyed by oxygen.

The assumption that CHCl_3 acts directly on the cerebral centre is not confirmed by experience. For those instances which would seem to support it are explained either by the intervention of mechanical obstruction, which obstructs normal oxygenation and prolongs the period of unconsciousness, or by the high degree of narcosis which has been attained.

But the readiness with which all the parts that are directly or indirectly affected by CHCl_3 -action regain their normal condition, and consequently their normal function, on its with-

drawal—the air-way being maintained normally patent—is evidence of the evanescent influence to which they are subjected by it. The causal factor which exercises a transitory effect upon tissue-life is $-\text{OXY}$. The changes which it effects in the muscles and in the cerebral centres begin to disappear when it ceases to operate, and they completely disappear when the blood is normally oxygenated. Thus, not only the results following upon CHCl_3 -action, but also the circumstances which characterise their progress, are in conformity with those of $-\text{OXY}$.

The conclusion, therefore, is that CHCl_3 acts directly on the blood, and that its result upon it is the removal of oxygen. The $-\text{OXY}$ -factor, which is their proximate cause, thus intermediates between the indirect phenomena and their ultimate cause, which is CHCl_3 .

The relation between CHCl_3 and the blood is twofold: its negative action causes deoxygenation by the diminishment of the normal supply of air to the alveoli, but this has been shown to be unequal within given limits to produce unconsciousness; it is the physiological or physiologico-chemical action of CHCl_3 that is indirectly the cause of the suspension of the functions of the cerebral centres. It is

possible, therefore, to limit the quantity of CHCl_3 -vapour that is absorbed to the amount of oxygen that is requisite to be abstracted from the blood. And inasmuch as the blood, which is the part directly affected by the physiological action of CHCl_3 , is a variant, and as its actual condition necessarily influences the result that appears in it, it follows that each individual example will require its own anæsthetic degree of CHCl_3 -action. But the administration of CHCl_3 may be (but it is not necessary that it should be) accompanied by undue interference with the function of the respiratory machine, proceeding from its negative and physical actions; and in the course of CHCl_3 -unconsciousness, mechanical obstruction may occur as an indirect consequence of CHCl_3 -action. The importance of taking the proper precautions to avoid the former and remove the latter in investigating the action of CHCl_3 , will at once be obvious when it is perceived that the effect of these abnormal factors tends to intensify CHCl_3 -results by increasing the deoxygenation of the blood. Their operancy, when unrecognised, will account for some of the irregularities which have been ascribed to the physiological action of CHCl_3 .

PART V.

EXPERIMENTAL INVESTIGATION.

§ 96. *EXPERIMENTAL treatment of blood with CHCl_3 .*—The ordinary atmosphere in which oxygen is diluted does not exercise any immediate influence on CHCl_3 . In certain circumstances, however, it is liable to undergo a change which is associated with impairment of its anæsthetic value. But it is to be observed that the intensity of the effect varies with the quantity of the cause, and it is known that nascent or pure oxygen causes oxidation of certain substances that are (practically) unaffected by it when its power is reduced by dilution.

I. The first change that appears on mixing fluid CHCl_3 with blood is an increase in the degree of its normal colour. It is immediately produced, and it is followed by greater or less diminution of the intensity of the charac-

teristic odour of CHCl_3 . This result, in so far as colour is concerned, is apparently contradictory to the conclusion which has been reached—viz., that CHCl_3 abstracts oxygen from the blood; for if $-\text{Ox}$ be the cause of discoloration, it would seem that the blood should become immediately darkened. But $-\text{Ox}$ is only one of the possible factors concerned in the discoloration of the blood, and its agency may be indirect. The other factors are the arrangement of the coloured blood-corpuscles, which, in the form of rouleaux, possess in a more efficient manner the power of reflecting and refracting light; and an assumed excess of CO_2 in the arterial blood. The vapour of the latter was therefore mixed with blood which had been treated with CHCl_3 . In some examples, the CHCl_3 -blood became at once discoloured, and presented the characters of venous blood. But in others, though the change was finally effected, yet it was not immediate; there was a period of transition, which varied in length, the longest being 10', in which discoloration proceeded gradually; and it was observed that as the CHCl_3 -blood became darker, it also became thinner in consistency—i.e., it approximated more to venous blood. No certain conclusion could be drawn

from these results. CO_2 may be prevented from entering into solution. On the other hand, its presence may tend to hasten the removal of oxygen.

In order to test the connection between the loss or diminution of CHCl_3 -odour and the blood, the following experiments were instituted: the quantity of normal blood was kept constant at one pint, but the amount of fluid CHCl_3 was made to vary. It was found that when the latter was small—*e.g.*, f. $\frac{3}{4}$ i—no trace of odour could be distinguished immediately after shaking; but with larger quantities, up to f. $\frac{3}{4}$ i, there was a diminution of intensity of odour, which was less as the proportion of CHCl_3 was greater.

But the duration of these experiments was limited. And the inference that might be drawn, that because there was no immediate discoloration, therefore there were no changes taking place to effect it ultimately, will be perceived to involve a curious error on considering the results of the following series of experiments conducted under different circumstances. The source of the error is in not recognising the resisting power which the blood possesses against the influences of an agent which are adverse to its wellbeing.

The same quantity of blood was treated with different quantities of fluid CHCl_3 and left to stand exposed to the air, so as to discover what might be the result of time on the changes appearing in it. After an interval which varied in length, it became darkened in all instances; but in some the degree of discoloration remained more or less stationary, while in others it manifested a progressive increase in the degree of its intensity, with less or greater rapidity, until it became black. At the same time that the blood was becoming more discoloured, it was losing in consistency, and a direct proportion was observed to exist between discoloration and fluidity—viz., as the degree of the former increased so did the degree of the latter. Thus, the final result on the initial CHCl_3 -arterial blood was its reduction to the condition of venous blood. In those instances in which it was produced more rapidly, it was observed that the quantity of CHCl_3 was larger, while it was smaller in those of less rapid occurrence.

But ordinary venous blood shaken with air becomes arterial. The blood affected by fluid CHCl_3 was therefore treated with air. But prolonged shaking, even when extended to 2° , failed to restore the colour. Microscopic exam-

ination of the CHCl_3 -blood showed that the coloured blood-corpuscles had lost their proper shape and had become crenated.

The self-preservation of the blood explains the fact that the action of CHCl_3 is not immediately manifested by an adverse change of its condition. On the other hand, the presence of CHCl_3 leads to the utmost efficiency in the defence of the blood against it, as is shown by the blood maintaining its normal consistency, and by the increase in the degree of its normal colour. The resisting power of the blood is gradually overcome, but when once broken through, it quickly yields to the continuous attack of CHCl_3 .

Now the circumstances under which these experiments were performed are not the same as those which obtain in the ordinary administration of CHCl_3 . There is a difference in the degree of local effect on the blood between CHCl_3 in the form of fluid and CHCl_3 in the form of vapour. And it is possible that fluid CHCl_3 may exercise a destructive influence on the oxygen-carriers. Secondly, the vapour of CHCl_3 , which is absorbed into the blood, and, as CHCl_3 -blood, is carried by the circulation to the various tissues, is the proper means of studying the purely physiological action of

CHCl_3 ; for not only is local, as distinguished from physiological, action thereby reduced to a minimum if it exists at all, but the quantitative factor can also be more minutely varied, and the progress of an experiment interrupted on the attainment of any particular degree of result without the appearance of any further change than that which is effected.

II. The following series of experiments were consequently instituted in order to discover the effect of CHCl_3 -vapour on the blood.

Two flasks with nozzles are put into communication by means of rubber tubing. Blood is poured into one, so as to fill it to the half of its capacity, and f. 3ii. CHCl_3 into the other. The apparatus being rendered air-tight, the warmth of one hand promotes the uniform evaporation of CHCl_3 , whilst the other continuously shakes the blood in order to change the surface of contact, and therefore hasten the absorption of the vapour. For the purpose of comparing differences of tint, a similar flask, containing precisely the same amount of blood, is kept air-tight.

The normal colour of the blood very quickly undergoes an increase in the degree of intensity, which it maintains for a period of 10'. It then begins to darken, and the degree of discoloration

progressively increases, until at the end of 45' it reaches the colour of mahogany. But the altered blood still preserves some degree of consistency, which it has been gradually losing, as is shown by the duration of the stain upon the neck of the flask. If at this stage the action of CHCl_3 -vapour is continued until the colour becomes black, and no trace of consistency remains, it will be impossible for the blood to recover its normal condition with the assistance of air. But if, on the contrary, the influence of the vapour is withdrawn, and the altered blood continuously shaken with air, this anomalous change will be presented,—it will become black and thin, and will exhibit all the characters of venous blood, with this single exception, that it does not readily absorb oxygen from the air and become quickly converted into arterial blood. But it will do so gradually, if the treatment of shaking it with air is continuously applied, and will present, but in the reverse order, exactly the same differences of tint as obtained when oxygen is abstracted from it. Thus, at the end of 5' it becomes mahogany-coloured, and acquires a certain degree of consistency. And as more oxygen is absorbed, the colour becomes less deep and the consistency greater, until at the end of

1° the blood appears to be restored to its normal condition. On microscopical examination no appreciable change could be detected in the coloured blood-corpuscles.

The blood which had thus been recovered from the effect of CHCl_3 was again subjected to its influence in the same way. And in order to determine whether any result was produced which had not been observed, a second experiment was simultaneously conducted with the former, but with blood which had not previously been affected by CHCl_3 .

The same series of changes were presented in both, but the rate of their progress was different in each, being more rapid in that in which the blood had already been influenced by CHCl_3 . Conversely, the rate of recovery was quicker in that in which the blood had not been affected by CHCl_3 . Thus, blood previously rendered venous by the action of CHCl_3 in 45', now required 30' for the same purpose, while its recovery took 1° 20'. As in the first, so in the second treatment of the blood with CHCl_3 , no appreciable change could be detected in the oxygen-carriers under the microscope.

The blood which had been twice consecutively treated by CHCl_3 was a third time subjected to its influence, a short interval only

elapsing between the experiments. In this series a marked diminution is seen in the resisting power of the blood; its colour becomes darkened at the end of 2', and black after an interval of 15'. And in no single instance did the normal colour return, though the treatment with air was continued beyond 2°. Microscopical examination showed that the coloured blood-corpuscles had lost their normal characters. The precautions which were taken to limit the degree of CHCl_3 -effect, so as to ensure recovery, were thus unsuccessful. For, though the vapour of CHCl_3 was withdrawn before the blood became as deeply discoloured as in the former series of experiments, the quantity remaining in solution was relatively excessive in regard to its resisting power. The inference may therefore be drawn that diminishment of the resisting power of the blood does not proceed at a uniform rate, but that it is gradually reduced at first, and afterwards quickly declines.

If, instead of fresh blood, experiments be made with blood that has been kept for some days, the removal of its oxygen by CHCl_3 will be found to be effected more rapidly. For example, blood five days old will manifest an obvious diminishment of resistance as compared with that which

it presented when fresh, and on the tenth day it will exhibit very little at all. The resistance which the blood, removed from its natural surroundings, opposes against agents that encroach on its vitality is thus very great. *A fortiori* it will be greater when in circulation.

If the vapour of CHCl_3 be withdrawn after the production of a given degree of discoloration and the blood treated with air, its colour, instead of diminishing as might be supposed, increases in intensity, after which it gradually returns to the normal. The source of the supply of the agent has been cut off; but a certain amount of it still remains in solution in the blood, and continues its effect until it is destroyed. The oxygen-carriers absorb oxygen from the air, and yield it in a nascent or pure condition to CHCl_3 . Thus they act as intermediaries between the latter and the atmosphere, and it is conceivable that their function may be impaired for the time being, owing to the abnormal conditions under which it is performed. The supposition would account for the slowness with which the blood is reoxygenated. The abnormality induced in the oxygen-carriers can, however, be only slight, inasmuch as they ultimately recover their normal function.

Pure oxygen might be used, or an atmosphere containing a larger proportion of oxygen than the normal, in recovering blood that has been rendered venous by the action of CHCl_3 . And if there be a larger proportion of oxygen present, the inference is that the rate of recovery will be accelerated. But the experiments have been confined to the use of air alone in recovering blood treated with CHCl_3 , for the reason that it is the natural means of supplying oxygen to the blood. In instances of CHCl_3 -narcosis, terminating in respiratory arrest, it is not so much the proportion of oxygen as the normal patency of the air-way that is of fundamental importance in the artificial restoration of the action of the respiratory machine.

CHCl_3 causes directly an abnormal condition of the blood, which is completely removed by the absorption of oxygen. The irresistible conclusion, therefore, follows that CHCl_3 abstracts oxygen from the blood. But in the process it is destroyed. Consequently the inference is that it is oxidised, and it is verified by the oxidation of CHCl_3 by H_2O_2 . That the products of CHCl_3 -oxidation are not injurious, either to the blood or to any other part of the organism, is proved by the return to their normal function of all the parts that are di-

rectly or indirectly affected by CHCl_3 after it has ceased to operate.

It will be seen, therefore, that it is impossible for CHCl_3 to remain in the blood without becoming oxidised. But if there be an excess in the circulation—*i.e.*, such an amount as will require more oxygen for its oxidation than can be supplied by the blood, without the latter manifesting any local indications of the alteration that is effected in it—the question will arise, What influence does that extra quantity exert, if any, upon the tissues of the organism, and particularly upon the cardiac muscle?

In the first place, the excess of CHCl_3 absorbed into the blood is not equivalent to the quantity that may be administered, but is determined by the negative action of CHCl_3 , which, by causing distension of the pulmonic artery, safeguards the blood against too rapid a rate of the process of deoxygenation. The quantity of CHCl_3 , though limited, may possibly be sufficient to exert a prejudicial local influence on the tissues, for the degree of intensity of the cause is one of the determinants of the result, and what a small proportion of CHCl_3 in the blood cannot effect in this respect, a larger one may be able to produce. It will be necessary, consequently, to inquire into the

phenomena that follow upon the presence of an excess of CHCl_3 in the blood. And in narcosis we find that while the frequency of respiration is accelerated, the frequency of the pulse is diminished and its tension increased. Now plus frequency of respiration is normally followed by plus frequency of the pulse. An opportunity, therefore, is provided to introduce the local influence of CHCl_3 as a causal factor in the explanation of the irregular condition of the pulse. If the source of the latter be ascribed to the heart, it will follow that the local action of CHCl_3 is associated with a greater degree of cardiac energy than the normal. If, however, it be assumed that the long-continued action of an excess of CHCl_3 in the blood ultimately causes cardiac failure, through its injurious influence on the cardiac muscle, the assumption leaves unexplained the over-distension of the right ventricle, which accompanies what may eventually prove to be only a temporary arrest of the cardiac function.

The amount of standard CHCl_3 needed to produce anæsthesia in a normal male adult is 3iiss, and if we subtract 3iss as the proportion that is lost by evaporation into the air, the vapour of 3ii will represent the quantity that affects the blood. Thus the ratio be-

tween the amount of CHCl_3 and the quantity of the blood, which may be taken as 10 lb., is very small. The end-object of administration is thus the production of a constant state of x -degree of deoxygenation, x representing the actual resisting power of the blood. And its attainment is practically effected by dividing the dose into equal parts, and administering them at frequent intervals; in other words, by maintaining the CHCl_3 -air atmosphere constant. The quantitative action of CHCl_3 will thus be perceived to occupy the foremost place in the method of its administration.

Limited to the anæsthetic degree of its action, CHCl_3 produces the least possible disturbance to the respiration, the pulse, and to nutrition generally. In these respects it possesses superior advantages to its allies, which are either more stimulant, and consequently more exhausting, or else their vapour is heavier. The density of CHCl_3 -vapour will provide the only solid argument against its being an ideal agent for inducing and maintaining unconsciousness. For the action of the respiratory machine is liable to undergo variations, which proceed from different sources. Consequently the possibility of a respiratory overdose arises. But that will be counteracted by equalling the pro-

portion of CHCl_3 in the CHCl_3 -air atmosphere to the requirements of the altered conditions of the respiratory machine.

The abstraction of its oxygen by CHCl_3 leads to the demonstration of the causation of the discoloration of the blood.

It has been shown that blood may be de-colourised without the intervention of CO_2 . The inference, therefore, is that CO_2 is not necessary to its causation.

It has also been shown that when oxygen is removed within a given limit of quantity, no discoloration takes place. On the contrary, its removal is associated with an increase in the degree of colour-intensity when CHCl_3 is the agent that is used to effect it. The inference, therefore, is that the abstraction of oxygen is not the direct cause of discoloration. But it is causally connected with it, for as the proportion of oxygen below the given limit diminishes the degree of discoloration increases, and as the proportion of oxygen increases the degree of discoloration diminishes. The consistency of the blood, however, presents a variation at the same time as discoloration, and the two variations are inversely proportioned to each other: thus, as the blood becomes more discoloured it is less consistent, and as it becomes less discoloured it

is more consistent. It will be essential, therefore, to introduce a cause that will explain not only the variation of colour, but also of consistency. The factor which invariably accompanies changes of colour and of consistency is the arrangement of the coloured blood-corpuscles. It is known that in arterial blood it takes the form of rouleaux, which oppose the passage of light. On the other hand, it is known that in venous blood the coloured blood-corpuscles are disparate, and consequently their power to reflect light is reduced to a minimum. In the intermediate stages between arterial and venous blood the rouleaux become broken up, and the process of their disintegration proceeds *pari passu* with the continuous removal of oxygen. Conversely, the absorption of oxygen is associated with their reconstruction. The conclusion, therefore, is that oxygen is the indirect cause of the discoloration and diminished consistency of the blood, and that it acts by causing the isolation of the oxygen-carriers.

Another point of importance is the source of the stimulation of the respiratory centre. In CHCl_3 -narcosis, on the assumption that there is an absolute excess of CO_2 in the blood, increased frequency of respiration is associated with $+\text{CO}_2$ and $-\text{OXY}$. But in CHCl_3 -anæ-

thetia it has been shown that there is no interference with aeration, and in these circumstances that is the only agency by which the CO_2 element in the blood can be affected. For the direct action of CHCl_3 is restricted to the oxygen constituent. Increased frequency of respiration is therefore associated, 1, with dark blood, which is known to contain less oxygen than normally, and assumed to contain an excess of CO_2 ; and, 2, also with normally coloured blood, which can only contain the normal proportion of CO_2 , and is proved to contain less than the normal amount of oxygen. The $-\text{OXY}$ -factor is thus proved to be a respiratory stimulant. Is it the only one? For it is conceivable that $+\text{CO}_2$ may also stimulate the respiratory centre. Now a cause can only produce its effect when it is in action. The first essential is to demonstrate that it is present, and it is the fact that the blood may be dark—*i.e.*, in the condition in which $+\text{CO}_2$ is supposed to be present—without there being any change of its proportion. But is the proportion of CO_2 in the arterial blood increased in the instance of a neutral agent displacing air? Now the factor that determines the alveolar circulation is the presence of oxygen in the alveoli. If CO_2 be capable of being absorbed, the fact has to be

explained why the alveolar circulation is retarded when the proportion of oxygen in the alveoli is reduced. But assuming that it is present in dark arterial blood, does it act as a stimulant of the respiratory centre? In order to decide that question, it will be necessary to estimate the amount of the $-OXY$ -factor in any given instance, and the degree of stimulation of the respiratory centre that accompanies it. If the degree of stimulation of the respiratory centre, as measured by the increased frequency of respiration, correspond exactly with the quantity of a cause—viz., $-OXY$, that is known to produce it—it will follow that a variation of the CO_2 element is not a respiratory stimulant; because it is impossible that a cause, assumed to be acting, shall not produce its effect; and it is not shown that CO_2 is prevented from coming into action. But if, on the contrary, the degree of result—viz., of respiratory acceleration—be proved to be greater than can be explained by the quantity of the $-OXY$ -factor present, the difference will obviously proceed from another causal factor co-operating with it, and that factor may be $+CO_2$.

§ 97. *Respirable vapours and the blood.*—Oxygen may conceivably be abstracted from the contents of the air-way. The vapour of

HCy is very diffusible and readily oxidisable. Its presence, therefore, in the air-way, will be followed by the disappearance of the oxygen in it, the consequence of which will be immediate and complete alveolar stasis. The action of the right ventricle will thus be opposed by a resistance in the terminals of the pulmonic artery, which is not more or less rapidly or gradually induced, but completely and suddenly. A proportion of HCy vapour is carried into the blood antecedently to alveolar stasis. And the increase in the intensity of the normal colour of the blood is explained by the effort of the coloured blood-corpuscles to preserve themselves from imminent destruction. But the fight for oxygen is unequally sustained, and eventually the corpuscles yield their oxygen, and the blood in the arteries becomes venous.

It is possible to abstract oxygen from the blood, by agents introduced into and circulating in it. And it is conceivable that it may be effected with or without injury to the oxygen-carriers. In the instance of CH_4 there would appear to be no harm caused by its presence in the blood. But in the case of CO, by virtue of its combination with hæmoglobin, there is a tendency to the destruction of the oxygen-carriers, and consequently to a shortage

in the general supply of oxygen to the tissues. The agent causing the abstraction of oxygen may, however, exert a different kind of effect on the coloured corpuscles, or if the same, it may produce it less rapidly than CO; thus the degree of the intensity of its action may be so limited as to cause no other disturbance in the constitution of the blood than that of the removal of a certain amount of its oxygen.

CHCl_3 and ether are typical examples of a group of agents which possess the power of abstracting oxygen without otherwise injuring the blood. All the members of it derive either from a CH_3 or C_2H_5 base. The density, and consequently the diffusibility, of their vapours varies: thus ether-vapour is comparatively light, while that of methylene bichloride is comparatively heavy, a circumstance which has to be considered in relation to the initial motor-power of the respiratory machine. But all of them are characterised by the decomposition which they undergo in the presence of pure oxygen, and it would appear that the products of their oxidation are inert. And from the fact that the action of ether is accompanied by a higher degree of respiratory acceleration than that of its allies, the inference may be drawn that the rate of its oxidation is more

rapid—*i.e.*, it is more easily oxidised than, *e.g.*, CHCl_3 .

The phenomena that accompany the action of all these agents are traced to $-\text{OXY}$ as their intermediate cause, with the single exception of the discoloration of the blood, which is the direct result of the agent. And the explanation of the differences that may appear in the course of their operation are referred, on the one hand, to their local influence on the action of the respiratory machine, and on the other to differences of quantity in the blood. It will be essential, therefore, to isolate the circumstances in which the blood is being deoxygenated by any particular agent.

Unconsciousness may be induced by the indirect action of agents which enter the blood, either from absorption by mucous membranes or directly from a wound. And it would appear that, in default of its excretion, the only means that nature provides to counteract, and in favourable circumstances to destroy, the prejudicial influence of an agent in the blood is oxidation. But there is no likeness with regard to chemical structure between opium, chloral, KBr and $\text{C}_2\text{H}_5\text{OH}$. They all agree, however, in this—*viz.*, that they are oxidised by pure oxygen. Some of them—*e.g.*, opium and

alcohol—exercise a particular local effect on the arteries of the mucous membrane, tending to constrict them. And this factor, in conjunction with the quantity of the contents of the stomach, where absorption is effected by means of that organ, is to be considered in estimating the rapidity with which they enter into the circulation. It has already been shown that the density of a vapour which is capable of being absorbed by the alveoli acts as a check to the rate of its absorption into the blood, and thus tends to prevent the accumulation of an undue amount of it in the circulation. So, in the instance of opium; its local action is the means whereby the rate of its introduction into the blood is diminished, and consequently it tends to prevent an undue and rapid effect upon it. This circumstance may explain why it is that the pupil remains contracted in the early stages of opium-narcosis. But eventually it becomes dilated and sluggish, and in these respects agrees with narcosis caused by CHCl_3 , ether, and alcohol. But, whatever may be its ultimate cause, the degree of narcosis is reduced by accelerating the action of the respiratory machine. And in some instances in which an excessive degree of narcosis is produced, and which, consequently, present a decline of the

power of that machine, artificial respiration will be indicated before breathing ceases, in order to subserve the maximum absorption of oxygen under the circumstances. Thus, in the case of a child aged 4, who was subjected to an overdose of brandy, with a view to the prevention of sea-sickness, artificial respiration was, *lege artis*, conducted for 4° before the respiratory muscles manifested the ordinary signs of the complete recovery of their function.

Recovery was effected in this example of narcosis by the artificial introduction of oxygen. It may also be effected in opium and CHCl_3 -narcosis, and will be, when the circumstances are favourable, by the same means. The arrest of the action of the respiratory machine, when it occurs as the terminal link in the chain of the phenomena of narcosis, is the result of the exhaustion of the respiratory muscles. In regard to vapours, it will be perceived to be followed by a salutary tendency, inasmuch as their absorption is interrupted. But in regard to agents that are absorbed by the stomach, the object of its occurrence does not appear to be so evident.

The comparative study of examples of narcosis leads to the following generalisation: all narcotic agents are oxidisable and cause all their results

(direct and indirect) by abstracting oxygen from the blood. They do not act directly upon the cerebral centres, but indirectly through the intermediation of the $-OXY$ -factor, which, it would appear, is the only known cause of the suspension of their functions. The value of the oxygen-carriers as forming the first line of defence against the influence of foreign agents circulating in the blood is also to be noted. Their power of self-preservation is very great. They regulate the action of the respiratory centre, and by their stimulant effect upon it, a tendency is set in motion to recover the oxygen of which they have been deprived. The means by which they effect it is a variation of the proportion of oxygen which they contain. Thus the condition of less than their normal volume of oxygen is invariably followed by increased frequency of respiration; and on the contrary, it is invariably diminished when the amount of oxygen is increased, and, in favourable circumstances, temporarily arrested, —relative or absolute apnœa.

The introduction of the $+CO_2$ factor into the causation of respiratory stimulation appears, therefore, to be the consequence of an erroneous inference. The blood in the veins of the body is black and thin, and is known to contain a large

proportion of CO_2 . But, because the arterial blood undergoes an analogous change of colour it cannot be inferred with certainty that it contains, in its altered state, more than the normal amount of CO_2 —if it contains any at all—for the reason that discoloration of the blood can be effected without its presence. The mistake arises, first, in inferring the wrong cause of a phenomenon—*i.e.*, that $+\text{CO}_2$ causes discoloration; and secondly, in assuming that it exists in deoxygenated arterial blood, from the partial resemblance which the latter presents to venous blood.

§ 98. *Causation of death in narcosis.*—The respiratory centre is relatively indestructible. It is stimulated by a diminishment of oxygen in the blood. If, then, it can be shown that no agent associated with respiratory stimulation exists but what is oxidisable, it will follow that there is only one mode of affecting the respiratory centre through the blood, and *that* by a variation of the proportion of its oxygen. Consequently, the action of respiratory stimulants will be indirect.

But the respiratory machine may become disabled in one or more of its component parts. The air-way may be partially obstructed, either mechanically or by the presence in excess of a

heavy vapour in it; or both these abnormal conditions, becoming causal factors, may combine and produce respiratory arrest. The lungs may also be physiologically congested, and when that abnormal condition is rapidly induced, it will lead to arrest of the action of the respiratory machine. But the condition which is apt to escape the proper consideration which is due to it, is the progressive diminishment of the tone of the respiratory muscles in the course of narcosis. For it is precisely this factor that determines the onset of respiratory arrest. The circumstances in which the motor-power of the respiratory machine becomes enfeebled and eventually exhausted are, 1, the performance of more than the ordinary amount of work; and, 2, shortage not only of the quantity of blood supplying the respiratory muscles, but also of the principal ingredient of it, in so far as it concerns them—viz., of oxygen.

Because the respiratory machine is disabled, or inactive, it cannot thence be properly inferred that the condition of the respiratory centre is abnormal, in the sense that it is directly affected by the action of the narcotic agent in use. In these circumstances, however, it may be in a condition of disturbance, but the source of the disturbance is independent of the agent.

The respiratory centre is inhibited or arrested by the act of volition. And voluntary inhibited or arrested respiration may concur with an abnormal condition of the respiratory machine, which has been induced by the agent. Thus, there may be an excess of CHCl_3 -vapour in the air-way which may excite voluntary respiratory arrest, during which unconsciousness appears and is rapidly followed by muscle-rigidity,—the consequence of the rapid diminution of the amount of oxygen in the blood. The jaws being fixed and the base of the tongue displaced backwards, mechanical obstruction results, and consequently the passage of air from the outside to the alveoli is interrupted.

But the respiratory centre is also inhibited or arrested by the abnormal action of the stomach. Stomachic inhibition of the action of the respiratory machine may occur either in anæsthesia or in narcosis, which varies in degree. And it may, in addition, be accompanied by a respiratory overdose, which may be either relative or absolute. The respiratory machine may thus present either or both of the following abnormal conditions when its action is reduced by the abnormal condition of the stomach: 1, a variant degree of physiological pulmonic congestion; and, 2, a variant degree of respiratory overdose. Both

are causal factors in the production of respiratory arrest.

Functional arrest of the action of the respiratory machine, at the end of a full inspiration, is the necessary antecedent to the act of vomiting. But a full inspiration will be prevented by a respiratory overdose, or by pulmonary congestion. If, therefore, either of these abnormal conditions be present when the expulsion of the contents of the stomach is about to take place, it will oppose, according to the degree of its intensity, a less or greater resistance to the intake of air: consequently the action of the respiratory machine will be arrested at some stage in the act of inspiration, and will continue arrested until the opposing cause is removed.

The heart may fail from some inherent defect, and thus be the cause of death. But fall of blood-pressure is antecedent to the reduced action of the heart when it is caused by reflex stimulation of the vaso-motor centre. The return of the blood from the portal to the main circulation is through the lungs, and the alveolar circulation is determined by the presence of oxygen. It will be obvious, therefore, that all interference with the alveolar circulation will be antagonistic to the recovery of the

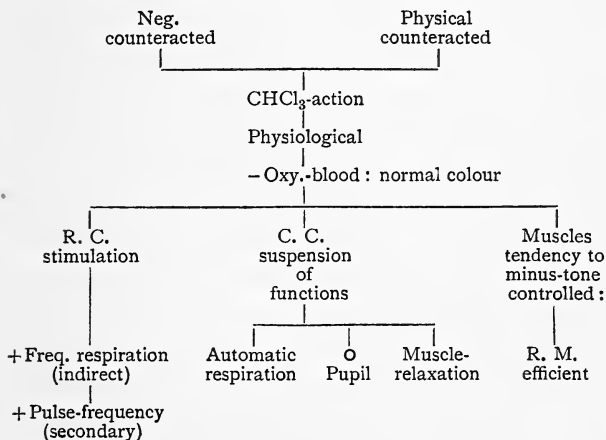
heart from the condition of reduced action, which is consequential upon primary fall of blood-pressure. And the causes of interference are mechanical obstruction in the air-way, respiratory overdose, and physiological pulmonic congestion.

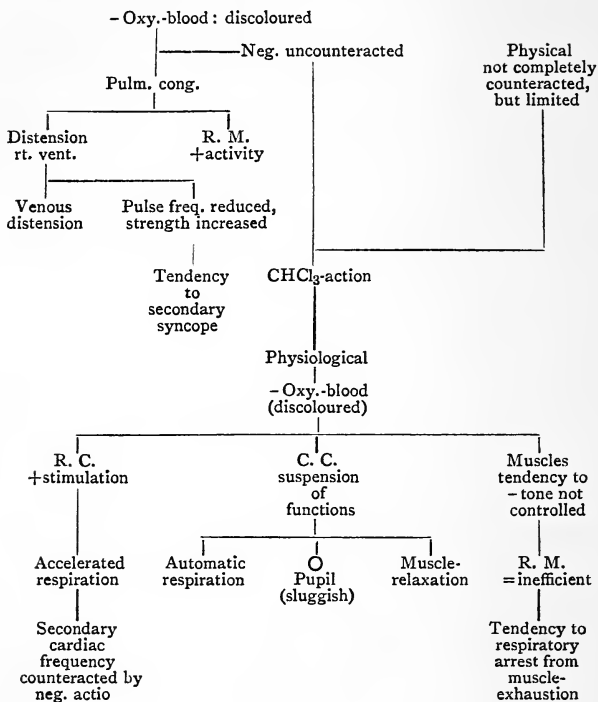
But in narcosis, which runs its course uncomplicated by vaso-motor, stomachic, or (primary) cardiac disturbance, the ultimate cause of death is oxygen-starvation. The respiratory muscles tend to become exhausted, and their failure to act forms a proximate cause: the action of the heart also tends to fail, and cardiac syncope, indirectly induced by the negative action of the agent when in the form of vapour, becomes the intermediary means of the causation of death. The question which fails first, the heart or the action of the respiratory machine, will be decided by the initial condition of the former. If the heart be abnormal, and, in consequence, less able than normally to withstand increased pressure in its right ventricle, it will fail before the respiration. But if the heart be normal, the action of the respiratory machine will cease before the pulse disappears, because the power of resistance possessed by the respiratory muscles is known to be less than that of the heart. (§ 82, p. 109.)

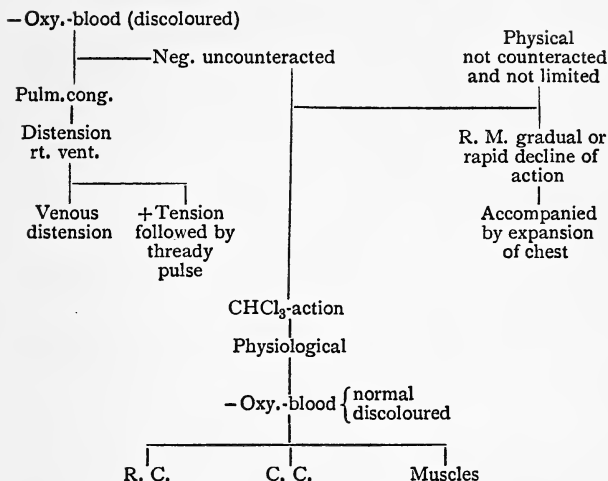
§ 99. *Scheme of the results of CHCl_3 -action.*

1. CHCl_3 -action $\left\{ \begin{array}{l} \text{negative.} \\ \text{physical.} \\ \text{physiological.} \end{array} \right.$

The following diagrams will serve to indicate the different origins of respiratory arrest and pulse-failure (excluding primary cardiac syncope) occurring during CHCl_3 -administration, as also to elucidate their causation.

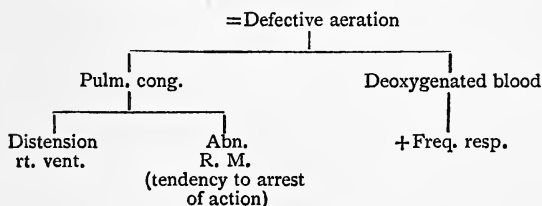
2. CHCl_3 -anæsthesia :—

3. CHCl_3 -narcosis :—

4. Respiratory overdose of CHCl_3 :—

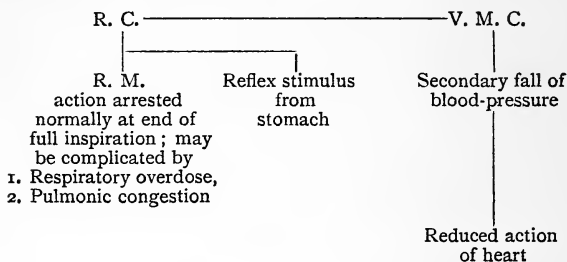
§ 100. *Scheme of the action of those agents which severally may complicate that of CHCl_3 .*

1. Mechanical obstruction :—

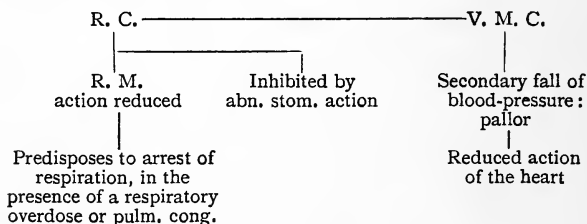


2. Abnormal stomachic action.

(a) Reflex or functional arrest of the activity of the respiratory centre :—

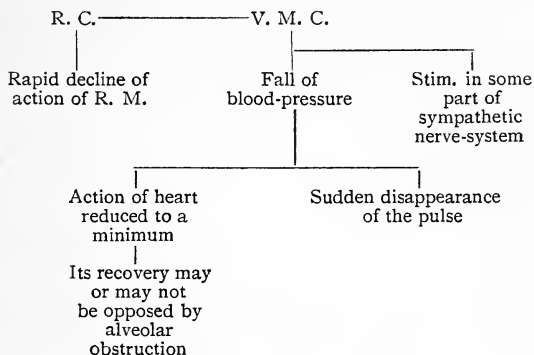


(b) Stomachic inhibition of the activity of the respiratory centre :—

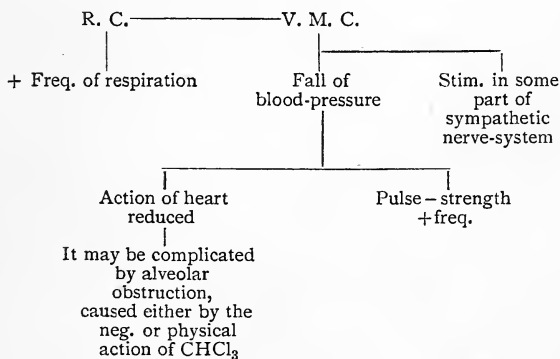


3. Reflex stimulation of the vaso-motor centre.

(a) Severe degree of—



(b) Moderate degree of—



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THE END.





